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Enantioselective divergent approaches to both (−)-platensimycin and (−)-platencin

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ABSTRACT

Enantioselective divergent approaches to (−)-platencin and (−)-platensimycin have been developed. A rationally designed chiral synthetic intermediate, possessing a useful α,β-unsaturated sulfone functionality, which served as a masked ketone as well as a good Michael acceptor, was successfully prepared via the highly enantioselective catalytic asymmetric intramolecular cyclopropanation (CAIMCP) developed in our laboratory.

1. Introduction

The emerging threat of multi-resistant bacteria, such as methicillinresistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), penicillin-resistant *Streptococcus pneumonia* (PRSP), and so on, has made researchers find new antibiotics having a new mode of action. Under such situation, the research group at Merck isolated new class antibiotics, (−)-platensimycin (**1**)[1] (Fig. 1) and (−)-platencin (**2**)[2] from *Streptomyces platensis* MA 7327 and 7339, respectively. (−)-Platensimycin (**1**) is a potent and selective inhibitor of FabF, the condensing enzyme, which catalyzes elongation in bacterial fatty acid synthesis.[1] (−)-Platencin (**2**) is a moderate inhibitor of both FabF and FabH, the enzyme catalyzing the initial condensation in bacterial fatty acid synthesis.[2] Because of their new modes of action, **1** and **2** show potent, broad-spectrum Gram-positive antibacterial activity, and also exhibit no cross-resistance to antibiotic-resistant bacteria, including MRSA and VRE.[1,2]

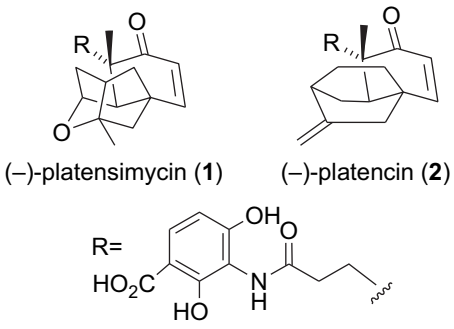

Fig. 1. Structures of (−)-platensimycin (**1**) and (−)-platencin (**2**).

These compounds have a same side-chain including 3-amino-2,4-dihydroxybenzoic acid as the common structure; however, both compounds have unique structural features in their polycyclic moieties. (−)-Platensimycin (**1**) has a tetracyclic framework including a cyclic ether while (−)-platencin (**2**) has a tricyclic framework, which consists of only carbons.

The new modes of action and unique structural features of these new antibiotics **1** and **2** have attracted much interest of synthetic chemists and medicinal scientists, and a number of research groups have reported total syntheses[3–6] and SAR studies.[7] Because of their novelty in the structure and biological activity, we were also interested in the enantioselective total synthesis of compounds **1**, **2**, and their new derivatives. The structural similarities between **1** and **2** led us to develop enantioselective divergent approaches to these antibiotics, and recently, we completed a formal total synthesis of **2**.[5] During the synthesis of **2**,[5] we found that the intermediate in the total synthesis of **2** would be used for the total synthesis of **1**, too. Therefore, we started the total syntheses of **1** via the same key intermediate, and herein report the full detail of the enantioselective formal total synthesis of **2** and a new enantioselective formal total synthesis of **1** via the enantioselective divergent approaches.

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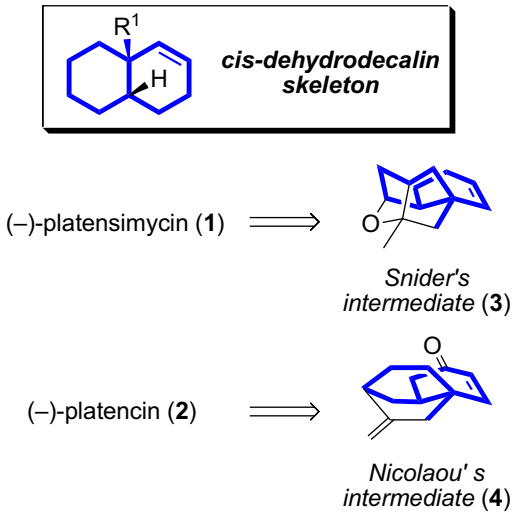
2. Results and discussions

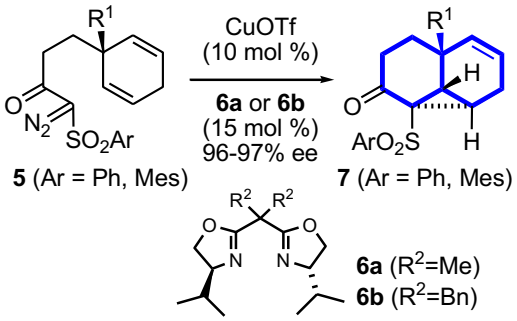
2.1. Retrosynthetic analysis of 1 and 2

In the course of the retrosynthetic analysis of **1** and **2**, we identified a common carbon framework, a *cis*-dehydrodecalin skeleton possessing a bridgehead stereogenic quaternary carbon, which was hidden within their structures (Scheme 1). The *cis*-dehydrodecalin skeleton was also found in intermediates reported earlier by other research groups, including Snider's intermediate **3**[3b] for **1** and Nicolaou's intermediate **4**[4a] for **2**. Therefore, we set **3** and **4** as targets of our formal total synthesis.



Scheme 1. *cis*-Dehydrodecalin skeleton hidden in **1** and **2**.

We have reported a highly enantioselective catalytic asymmetric intramolecular cyclopropanation (CAIMCP) of α-diazo-β-keto sulfones with CuOTf and bisoxazoline ligand **6**.[8] The cyclopropanes thus prepared have been successfully utilized for the enantioselective total synthesis of some natural products in our laboratory.[9] Indeed, tricyclo[4.4.0.0]decene derivatives **7** have been easily prepared in a highly enantioselective manner from **5** by the CAIMCP (Scheme 2).

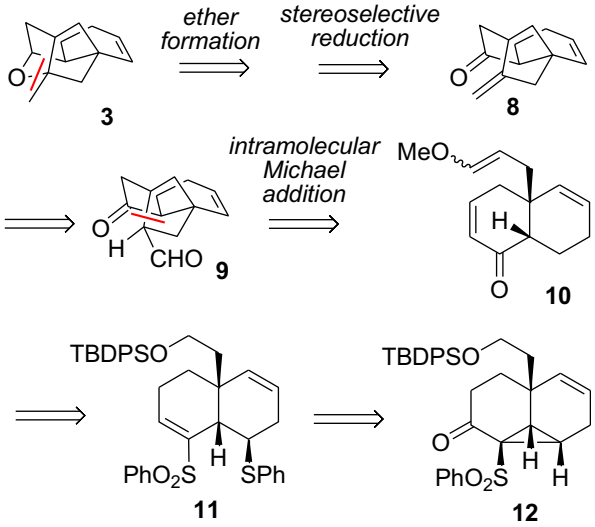


Scheme 2. Preparation of **7** by catalytic asymmetric intramolecular cyclopropanation (CAIMCP).

Compounds **7** can serve as key synthetic intermediates because they possess useful functional groups including a cyclopropane, an alkene, and a ketone. As compounds **7** incorporate the above mentioned *cis*-dehydrodecalin skeleton with a quaternary stereogenic center; hence, we surmised that **7** would be suitable for the synthesis of **3** and **4**, and undertook retrosynthetic analysis of **3** and **4** starting from **7**.

2.2. Retrosynthetic analysis of 3

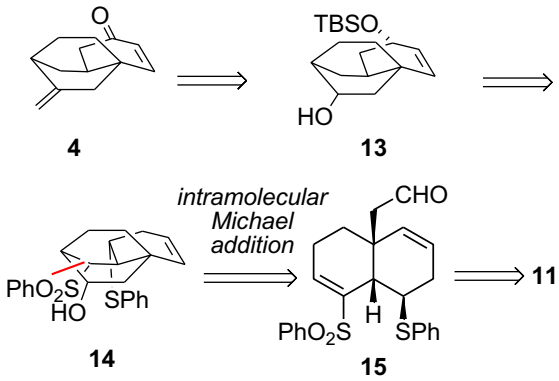
In our retrosynthetic analysis of **3** (Scheme 3), compound **3** would be formed by the acid-catalyzed intramolecular ether formation of the corresponding alcohol, which would be obtained by the stereoselective reduction of ketone **8**. Ketone **8** could be derived from keto-aldehyde **9** by converting the aldehyde group to the *exo*-methylene. We proposed that tricyclic keto-aldehyde **9** could be obtained by the acid-catalyzed intramolecular Michael reaction of ketone **10** or the corresponding aldehyde, which would be obtained from compound **11** since an α,β-unsaturated sulfone can be converted to a ketone and a C-1 elongation of the bridgehead substituent of **11** would furnish the methyl alkenyl ether moiety in **10**. Compound **11** was thought to be prepared via the ring-opening reaction of cyclopropane **12** and following appropriate transformations.



Scheme 3. Retrosynthetic analysis of **3**.

2.3. Retrosynthetic analysis of 4

Our retrosynthetic analysis of **4** is shown in Scheme 4. Compound **4** was thought to be formed from alcohol **13** via oxidation, Wittig olefination, deprotection of the TBS group, and oxidation of the resulting alcohol. Alcohol **13** would be obtained from **14** by reductive removal of all the sulfur-containing functional groups at the same time, followed by allylic oxidation to introduce the hydroxy group, and selective TBS ether formation. As an α,β-unsaturated sulfone is a good Michael acceptor, tricyclic compound **14** could be formed by the intramolecular Michael addition of aldehyde **15**. Finally, aldehyde **15** would be easily prepared from

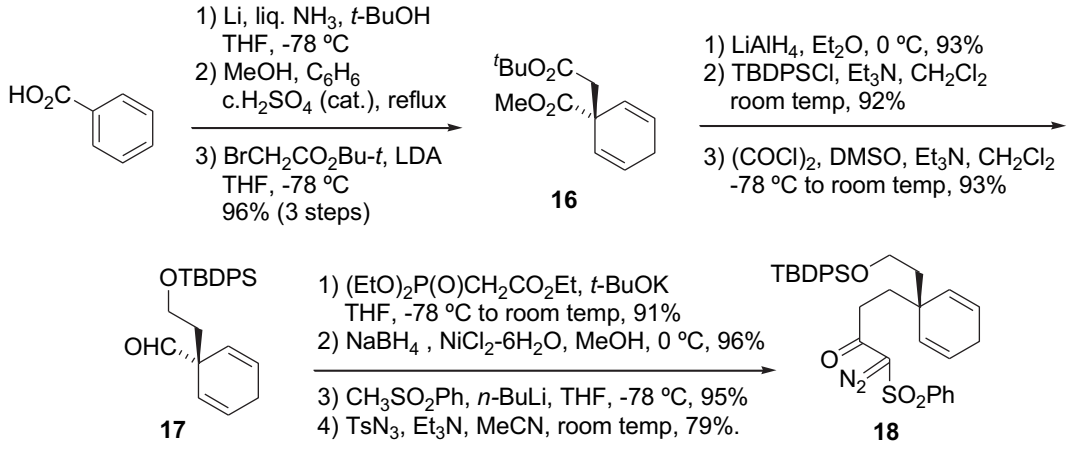


Scheme 4. Retrosynthetic analysis of **4**.

compound **11**, which is the same intermediate appeared in the retrosynthetic analysis of **3** (Scheme 3).

2.4. Preparation of α-diazo-β-keto sulfone 18

On the basis of the retrosynthetic analyses of **3** and **4** (Schemes 3 and 4), we first prepared α-diazo-β-keto sulfone **18**, which would afford cyclopropane **12** by the CAIMCP (Scheme 5). Birch reduction of benzoic acid to afford cyclohexa-2,5-dienecarboxylic acid **A**, formation of the methyl ester **B**, and subsequent alkylation of the enolate with *tert*-butyl bromoacetate afforded compound **16**. Reduction of diester **16** with $LiAlH_4$ afforded the corresponding diol **16a**, followed by selective TBDPS ether **16b** formation and then Swern oxidation to afford aldehyde **17**. Aldehyde **17** was subjected to Horner–Wadsworth–Emmons reaction to afford the α,β-unsaturated ester **17a**, followed by reduction with $NaBH_4$ in the presence of $NiCl_2$ to give the corresponding alcohol **17b**[10] formation of a keto sulfone **17c**, and diazo transfer reaction to afford α-diazo-β-keto sulfone **18**.



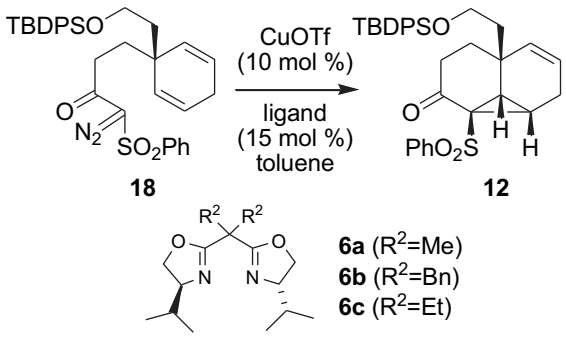
Scheme 5. Preparation of α-diazo-β-keto sulfone **18**.

2.5. CAIMCP of α-diazo-β-keto sulfone 18

The CAIMCP of α-diazo-β-keto sulfone **18** was examined using CuOTf and ligand **6a**–**c**. The CAIMCP of compound **18** with ligand **6a** proceeded at room temperature to successfully afford cyclopropane **12** (72%) with 95% ee (Table 1). The absolute configuration of **12** was not determined at this stage but was provisionally assigned as shown in Table 1 according to our transition state model.[8a] As shown in Table 1, the CAIMCPs with other ligands, **6b** and **6c**, were also examined. The ees were almost the same as that in entry 1, but the reactions proceeded slowly, required heating, and yields were lowered. These reduced reaction rate and yields were probably attributed to the crowded transition states that arose from the bulky substituent in the ligands **6b** and **6c**.

It should be noted that the attempted CAIMCP of compound **18a** (Fig.2) afforded the corresponding cyclopropane in low yield because a certain amount of by-products formed. This result indicates that the alkenylsilane in **18a** could be involved in the intra- or intermolecular reaction of the carbene complex formed from **18a**. The product obtained by the CAIMCP of **18a** was a potent candidate for the synthesis of **4**, but the low yield turned our attention to use compound **12**.

Table 1
CAIMCP of α-diazo-β-keto sulfone **18**



Entry	Temp (°C)	Time (h)	Yield[a] (%)	Ee[b] (%)
1	rt	11	72	95
2	rt, 50[c]	3.5, 15[c]	50	93
3	rt, 50[c]	3.5, 13[c]	42	93

[a] Isolated yields.
[b] Ee determined by HPLC. For HPLC conditions, see Supplementary data.
[c] Reaction was carried out at the indicated temperatures for the indicated times, respectively.

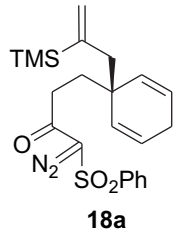
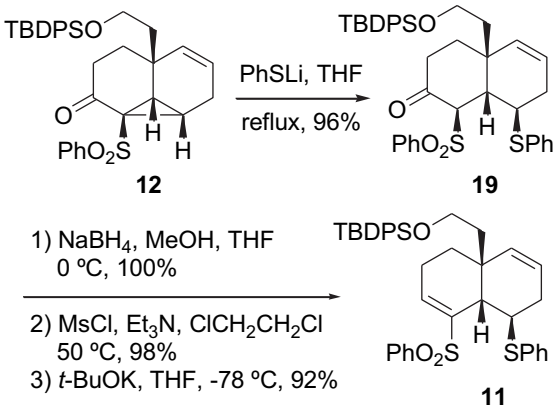


Fig. 2. Structure of **18a**.

2.6. Preparation of key intermediate 11

We first attempted the ring-opening reaction of cyclopropane **12** without removing the phenyl sulfonyl group; however, all the reactions with various reducing agents provided a mixture of products that lacked the phenyl sulfonyl group. Consequently, we conducted the ring-opening reaction of cyclopropane **12** with lithium thiophenoxide[9a] with the intention of removing the phenyl sulfide at a later stage. The ring-opening reaction with lithium thiophenoxide afforded the keto sulfide **19** in high yield (Scheme 6), and subsequent reduction with $NaBH_4$ afforded the corresponding alcohol **19a**. Dehydration of the resultant alcohol was attempted under various conditions, but unfortunately, a mixture of regioisomeric alkenes was always obtained. After several attempts, we found that careful treatment of its mesylate **19b** with potassium *tert*-butoxide at −78 °C successfully afforded alkene **11**.



Scheme 6. Preparation of **11** from **12**.

2.7. Formal total synthesis of (−)-platencin (2)

With the key compound **11** in hand, we first examined synthesis of compound **4** prior to the synthesis of **3**, because we thought that **4** would be more easily accessed from compound **11** (Scheme 7). Not only did removal of the TBDPS group in compound **11** with TBAF cause migration of the double bond, but use of TBAF with acidic additive was unsuccessful. Fortunately, the reaction with HF·py proceeded cleanly afforded the desired alcohol and kept the alkene intact, and subsequent Swern oxidation afforded aldehyde **15**.

The key reductive radical cyclization of aldehyde **15** with SmI_2 proceeded smoothly at 0 °C to afford compound **14**, which possessed the tricyclic core of (−)-platencin (**2**) as a single isomer. Treatment of compound **14** with lithium naphthalenide removed the sulfide and sulfone simultaneously without problem. Subsequent allylic oxidation with selenium dioxide followed by selective protection of the reactive allylic hydroxyl with TBSCl at −20 °C afforded TBS ether **13**. Dess–Martin oxidation of alcohol **13**, Wittig methylenation, removal of the TBS group, and Dess–Martin oxidation in the presence of sodium bicarbonate successfully afforded compound **4**.

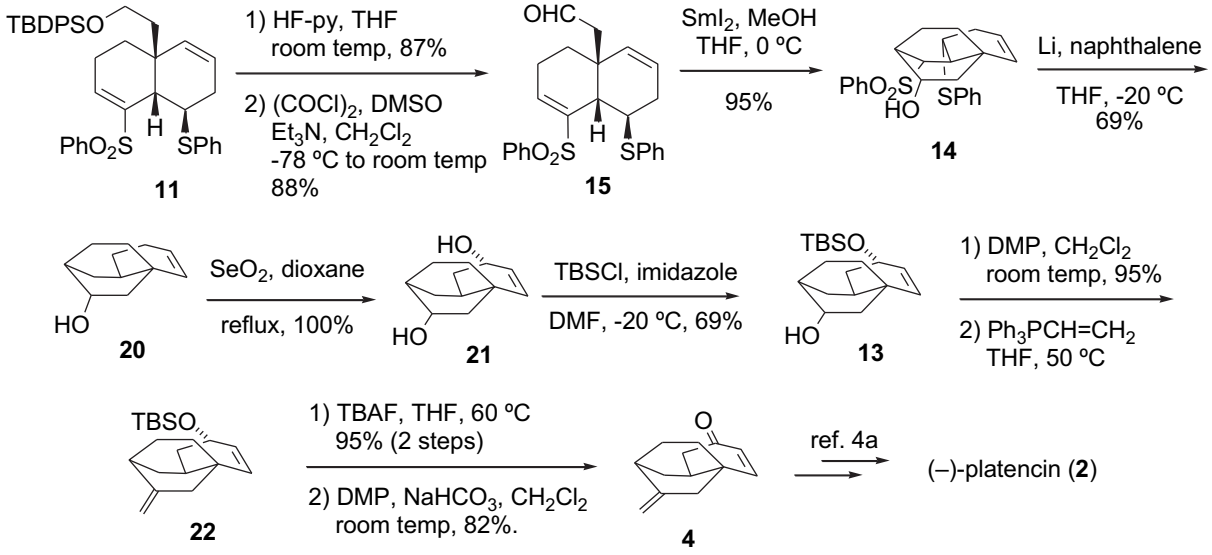
The synthesized compound was proved to be identical in all respects to the intermediate **4** described by Nicolaou (^1H and ^{13}C NMR, IR, MS, and $[\alpha]_D$).[4f] This fact established the absolute structure of cyclopropane **12** and verified the formal enantioselective total synthesis of (−)-platencin (**2**).

2.8. Formal total synthesis of (−)-platensimycin (1)

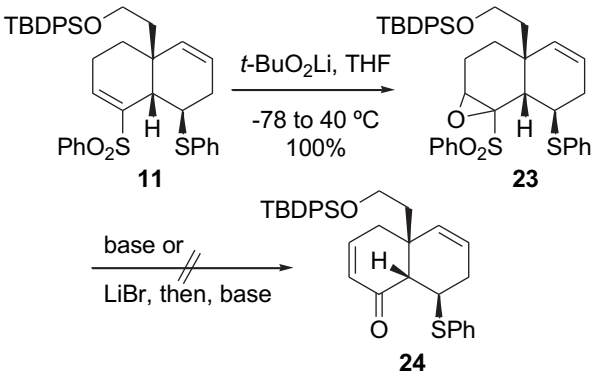
We next examined the formal total synthesis of (−)-platensimycin (**1**). Synthesis of compound **3** commenced with compound **11** because the α,β-unsaturated sulfone was thought to be converted to enone **24** via epoxide **23** (Scheme 8). The chemoselective epoxidation of compound **11** was realized using lithium *tert*-butyl hydroperoxide to afford the epoxide **23**; however, treatment of epoxide **23** with base caused no reaction. The reaction of **23** with lithium bromide induced epoxide-opening reaction at the less-hindered side to afford the corresponding α-bromo ketone, but which was not suffered from base-induced dehydrobromination.

Fortunately, treatment of epoxide **23** with magnesium iodide[11] afforded ketone **25** in 82% yield (Scheme 9). Removal of the sulfide with Raney-nickel and removal of the TBDPS group with TBAF gave alcohol **26**, followed by Swern oxidation and Wittig reaction to afford compound **27**.

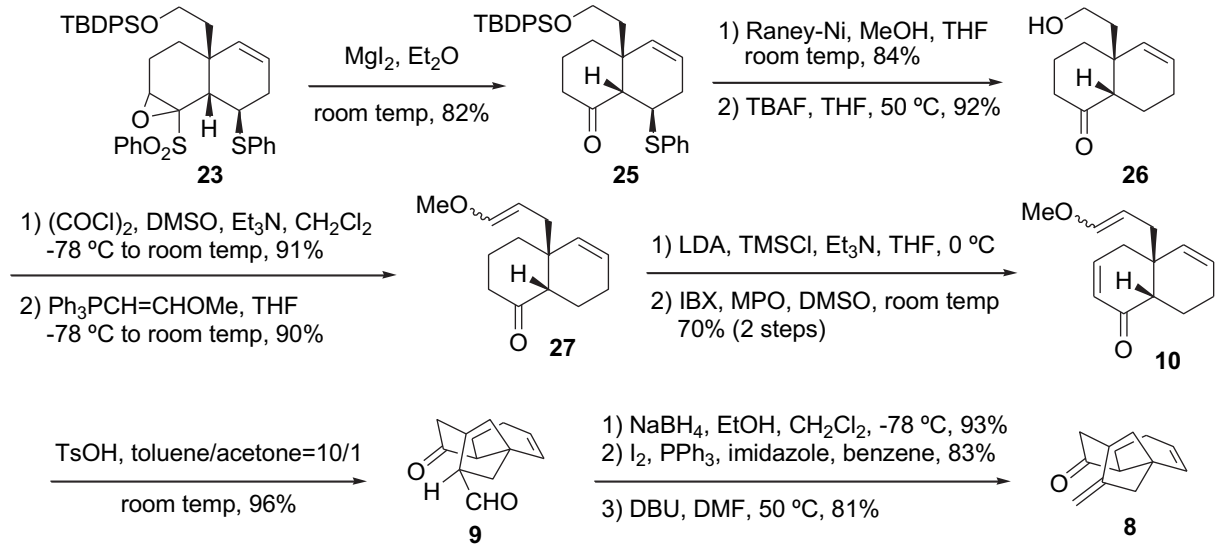
Introduction of the double bond into compound **27** was successfully achieved by Nicolaou's protocol[12] to afford enone **10**. We initially attempted to convert compound **10** to the corresponding aldehyde by hydrolysis under acidic conditions; however, we found that a mixture of products including compound **9** was obtained. After several attempts, the reaction of enone **10** in the presence of *p*-toluenesulfonic acid in a mixed solvent system (acetone and toluene) at room temperature was found to efficiently afford desired tricyclic compound **9**.



Scheme 7. Formal total synthesis of (−)-platencin (**2**).



Scheme 8. Attempted preparation of ketone **24** via epoxide **23**.



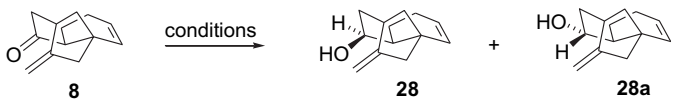
Scheme 9. Preparation of **8**.

Conversion of aldehyde **9** to ketone **8** via the enol triflate of **9** was very difficult because of the instability of the enol triflate. Therefore, following three steps sequence were employed. Thus, selective reduction of the aldehyde **9** in the presence of the ketone was achieved with $NaBH_4$ at −78 °C to provide the corresponding alcohol **9a**, which was converted to the iodide **9b**, and subsequent treatment with DBU furnished ketone **8**.

Reduction of ketone **8** was expected to afford **28** in a stereoselective manner due to the cage-like structure of **8** (Table 2). However, reduction with sodium borohydride gave **28a** as the major product (entry 1), and the ratio of **28a** increased in the reduction with DIBAL-H (entry 2). To deliver a hydride to the less-hindered side of the carbonyl group in **8**, more bulky reducing agents were examined. The ratio of **28**/**28a** was expectedly improved by use of L-Selectride, but the **28**/**28a** ratio was 1/1 (entry 3). Use of K-Selectride in THF further improved the **28**/**28a** ratio to 5/1 (entry 4), and finally, the reduction with K-Selectride in CH_2Cl_2 successfully afforded **28** as the sole product in high yield (entry 5).

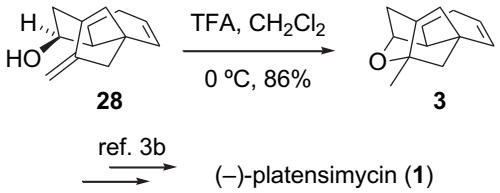
The obtained alcohol **28** was treated with TFA in CH_2Cl_2 to furnish the required ether bond, affording compound **3** (Scheme 10). The synthesized compound was proved to be identical with Snider's intermediate **3**[3b] in all respects (^1H and ^{13}C NMR, IR, and MS).[13] Compound **3** was synthesized from compound **11**, absolute structure of which had been determined in the synthesis of **4**, and absolute structures between **1** and **2** have been correlated; hence, formal enantioselective total synthesis of (−)-platensimycin (**1**) has been achieved.

Table 2
Stereoselective reduction of ketone **8**



Entry	Reagent (equiv)	Solvent	Temp (°C)	Time (h)	Yield[a] (%)	Ratio[b] **28**:**28a**
1	$NaBH_4$ (10.0)	MeOH	0	0.5	quant	1:2
2	DIBAl-H (2.0)	CH_2Cl_2	−78	0.5	quant	1:10
3	L-Selectride (1.5)	THF	−78 to 0	1.5	92	1:1
4	K-Selectride (6.0)	THF	−78 to 0	3.5	quant (at 72% conv)	5:1
5	K-Selectride (5.0)	CH_2Cl_2	−78 to 0	1.5	quant	1:0

[a] Isolated yields.
[b] Ratio determined by 400 MHz ^1H NMR.



Scheme 10. Formal total synthesis of (−)-platensimycin (**1**).

3. Conclusion

In summary, enantioselective divergent approaches to both (−)-platensimycin (**1**) and (−)-platencin (**2**) have been developed via the rationally designed common chiral synthetic intermediate **11**, possessing a useful α,β-unsaturated sulfone functionality, which served as a masked ketone as well as a good Michael acceptor. This intermediate **11** was derived from compound **12**, which was successfully prepared via the highly enantioselective CAIMCP we have developed. Therefore, the formal enantioselective total syntheses reported herein prove the applicability of uniquely functionalized tricyclo[4.4.0.0]decene derivative **12** as well as the usefulness of the CAIMCP in natural product synthesis. Although the enantioselective approaches to **1** and **2** described herein are not the shortest ones among the total syntheses reported to date, the chiral intermediate prepared by us enabled total syntheses of both **1** and **2**; therefore, it would be useful for the preparation of their new derivatives as well as for the enantioselective total synthesis of their congeners including the *cis*-dehydrodecaline skeleton that could emerge in the future.

4. Experimental

4.1. General procedures

^1H and ^{13}C NMR spectra were recorded on a JEOL AL-400 spectrometer or Bruker AVANCE 600 spectrometer. ^1H and ^{13}C chemical shifts are reported in parts per million downfield from tetramethylsilane (TMS, δ scale) with the solvent resonances as internal standards. The following abbreviations were used to explain the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; band, several overlapping signals; br, broad. IR spectra were recorded on a JASCO FT/IR-8300. Optical rotations

were measured using a 2 mL cell with a 1 dm path length on a JASCO DIP-1000. Mass spectra and elemental analyses were provided at the Materials Characterization Central Laboratory, Waseda University. All reactions were carried out under an argon atmosphere with dry, freshly distilled solvents under anhydrous conditions, unless otherwise noted. All reactions were monitored by thin-layer chromatography carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light as visualizing agent and phosphomolybdic acid and heat as developing agents. E. Merck silica gel (60, particle size 0.040–0.063 mm) was used for flash chromatography. Preparative thin-layer chromatography (PTLC) separations were carried out on self-made 0.3 mm E. Merck silica gel plates (60F-254). THF and Et_2O were distilled from sodium/benzophenone ketyl. Toluene was distilled from sodium. MeOH was distilled with a small amount of magnesium and I_2. Benzene and CH_3CN were distilled from CaH_2, and all other reagents were purchased from commercial sources.

4.2. Cyclohexa-2,5-dienecarboxylic acid (A)

To a stirred solution of benzoic acid (30.0 g, 0.25 mol) and *t*-BuOH (26.1 mL, 0.27 mol) in dry THF (65 mL) and liq. NH_3 (120 mL) at −78 °C was added lithium (5.11 g, 0.74 mol) in small pieces. The dark blue mixture was stirred at this temperature for 1 h. After the reaction was completed, to the reaction mixture was added to solid NH_4Cl until the blue color was disappeared, and the resulting mixture was slowly warmed to room temperature to remove NH_3. Then, H_2O (500 mL) and 2 N-HCl were added and the aqueous layer was extracted with Et_2O (200 mL×2) under acidic conditions (pH 2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The crude carboxylic acid **A** was used for the next step without further purification.

*4.2.1. Methyl cyclohexa-2,5-dienecarboxylate (**B**).* To a stirred solution of crude **A** in benzene (818 mL) were added MeOH (38.9 mL, 0.98 mol) and H_2SO_4 (3.6 mL, 67.5 mmol), and the reaction mixture was refluxed for 5.5 h. The reaction was quenched with saturated aqueous Na_2CO_3 (20 mL), and the aqueous layer was extracted with Et_2O (200 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by short column chromatography (hexane/ethyl acetate=3/1) to afford ester **B**, which was used for the next step without further purification.

*4.2.2. Methyl 1-(2-tert-Butoxy-2-oxoethyl)cyclohexa-2,5-dienecarboxylate (**16**).* To a stirred solution of DIPA (37.9 mL, 0.27 mol) in THF (818 mL) was added *n*-BuLi (1.59 M in hexane, 170 mL, 0.27 mol) at 0 °C and the solution was stirred at this temperature for 15 min. Then, the solution was cooled to −78 °C and a solution of crude **B** in THF (20 mL) was added via a cannula. After the reaction mixture was stirred at −78 °C for 30 min, *tert*-butyl bromoacetate (36.3 mL, 0.25 mol) was added, and the mixture was stirred at this temperature for 1 h. The reaction was quenched with saturated aqueous NH_4Cl (20 mL), and the aqueous layer was extracted with Et_2O (200 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=30/1) to afford diester **16** (56.4 g, 96% (three steps)) as a colorless oil; R_f 0.36 (hexane/ethyl acetate=10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.90 (2H, ddd, J=10.5, 3.3, 3.3 Hz), 5.80 (2H, ddd, J=10.5, 2.0, 2.0 Hz), 3.72 (3H, s), 2.70–2.65 (2H, m), 2.65 (2H, s), 1.42 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 169.5, 126.5, 126.0, 80.8, 52.3, 45.9, 45.7, 27.9, 25.9; IR (neat) ν_{max} 2979, 2952, 1732, 1637, 1153 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{14}H_{21}O_4$: 253.1440, found: 253.1441.

*4.2.3. 2-(1-(Hydroxymethyl)cyclohexa-2,5-dienyl)ethanol (**16a**).* To a stirred suspension of $LiAlH_4$ (80%, 23.3 g, 0.49 mol) in Et_2O (780 mL) was added **16** (55.8 g, 0.23 mol) at 0 °C and the reaction mixture was stirred at this temperature for 1 h. The reaction was quenched with saturated aqueous Na_2SO_4 and 2 N-HCl (100 mL), and the aqueous layer was extracted with Et_2O (100 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=1/1) to afford diol **16a** (36.1 g, 93%) as a white solid; R_f 0.11 (hexane/ethyl acetate=1/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.01 (2H, ddd, J=10.4, 3.4, 3.4 Hz), 5.52 (2H, ddd, J=10.4, 2.0, 2.0 Hz), 3.69 (2H, t, J=6.6), 3.38 (2H, s), 2.72–2.68 (2H, m), 1.61 (2H, t, J=6.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 129.5, 126.8, 70.2, 59.5, 41.4, 39.8, 26.4; IR (KBr) ν_{max} 3312, 2943, 2861, 1633, 1039, 1004 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_9H_{15}O_2$: 155.1072, found: 155.1067; mp 72–75 °C.

*4.2.4. (1-(2-(tert-Butyldiphenylsilyloxy)ethyl)cyclohexa-2,5-dienyl) methanol (**16b**).* To a stirred solution of **16a** (228 mg, 1.48 mmol) in CH_2Cl_2 (15 mL) were added Et_3N (0.41 mL, 2.96 mmol) and TBDPSCl (3.8 mL, 1.48 mmol) at room temperature. Then the reaction mixture was stirred at this temperature for 12 h. The reaction was quenched with saturated aqueous NH_4Cl (5 mL), and the aqueous layer was extracted with CH_2Cl_2 (5 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=20/1) to afford silyl ether **16b** (534 mg, 92%) as a colorless oil; R_f 0.44 (hexane/ethyl acetate t=4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66–7.64 (4H, m), 7.44–7.35 (6H, m), 5.84 (2H, ddd, J=10.4, 3.4, 3.4 Hz), 5.37 (2H, ddd, J=10.4, 2.0, 2.0 Hz), 3.66 (2H, t, J=7.1 Hz), 3.34 (2H, s), 2.68–2.46 (2H, m), 1.60 (2H, t, J=7.1 Hz), 1.03 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.6, 133.7, 129.6, 127.6, 127.0, 70.2, 60.8, 41.6, 40.0, 26.8, 26.5, 19.1; IR (neat) ν_{max} 3409, 2956, 2858, 1589, 1111, 1086, 823, 739, 702 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{25}H_{33}O_2Si$: 393.2250, found: 393.2233.

*4.2.5. 1-(2-(tert-Butyldiphenylsilyloxy)ethyl)cyclohexa-2,5-dienecarbaldehyde (**17**).* To a stirred solution of oxalyl chloride (18.5 mL, 0.212 mol) in CH_2Cl_2 (950 mL) was added DMSO (20.5 mL, 0.289 mol) at −78 °C and the reaction solution was stirred at this temperature for 15 min. Then, to the mixture was added a solution of **16b** (75.7 g, 0.193 mol) in CH_2Cl_2 (50 mL) via a cannula. After stirred at −78 °C for 15 min, Et_3N (67.2 mL, 0.483 mol) was added at this temperature and the mixture was stirred at room temperature for 30 min. The resulting mixture was quenched with brine (200 mL). The aqueous layer was extracted with CH_2Cl_2 (200 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=20/1) to afford aldehyde **17** (69.9 g, 93%) as a colorless oil. R_f 0.51 (hexane/ethyl acetate=4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.33 (1H, s), 7.66–7.57 (4H, m), 7.44–7.36 (6H, m), 5.95 (2H, ddd, J=10.5, 3.2, 3.2 Hz), 5.45 (2H, d, J=10.5 Hz), 3.67 (2H, t, J=6.8 Hz), 2.72–2.60 (2H, m), 1.93 (2H, t, J=6.8 Hz), 1.02 (9H, 2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.0, 135.6, 133.6, 129.6, 128.1, 127.6, 124.6, 60.3, 52.4, 37.8, 26.7, 26.5, 19.1; IR (neat) ν_{max} 2931, 2858, 2817, 2703, 1722, 1589, 1111, 823, 373, 702 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{25}H_{31}O_2Si$: 391.2093, found: 391.2093.

*4.2.6. (E)-Ethyl 3-(1-(2-(tert-Butyldiphenylsilyloxy)ethyl)cyclohexa-2,5-dienyl)acrylate (**17a**).* To a stirred suspension of *t*-BuOK (33.1 g, 0.251 mol) in THF (850 mL) were added ethyl diethylphosphnoacetate (56.8 mL, 0.286 mol) at −78 °C, and then, **17** (69.9 g, 0.180 mol). After the addition, a cooling bath was removed and the reaction mixture was stirred at room temperature for 1 h. The reaction was quenched with saturated aqueous NH_4Cl (100 mL), and the aqueous layer was extracted with Et_2O (50 mL×2). The combined organic layer was dried over Na_2SO_4,

filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=50/1) to afford α,β-unsaturated ester **17a** (74.6 mg, 91%) as a colorless oil; R_f 0.29 (hexane/ethyl acetate=30/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65–7.63 (4H, m), 7.43–7.26 (6H, m), 6.83 (1H, d, *J*=15.9 Hz), 5.73 (2H, ddd, *J*=10.2, 3.2, 3.2 Hz), 5.68 (1H, d, *J*=15.9 Hz), 5.38 (2H, d, *J*=10.2 Hz), 4.16 (2H, q, *J*=7.1 Hz), 3.65 (2H, t, *J*=7.6 Hz), 2.56–2.51 (2H, m), 1.77 (2H, t, *J*=7.6 Hz), 1.27 (3H, t, *J*=7.1 Hz) 1.02 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 154.1, 135.6, 133.8, 129.5, 128.8, 127.6, 125.0, 119.0, 60.9, 42.7, 41.3, 26.8, 26.0, 19.0, 14.2; IR (neat) ν_{max} 2931, 2858, 1716, 1644, 1589, 1110, 823, 741, 702 cm^{-1}; FAB HRMS $[M+Na]^+$ calcd for $C_{29}H_{36}O_3SiNa$: 483.2331, found: 483.2334.

*4.2.7. Ethyl 3-(1-(2-(tert-Butyldiphenylsilyloxy)ethyl)cyclohexa-2,5-dienyl)propanoate (**17b**).* To a stirred solution of **17a** (250 mg, 0.545 mmol) in MeOH (6 mL) were added $NiCl_2\cdot 6H_2O$ (19.4 mg, 0.0817 mmol) and $NaBH_4$ (22.7 mg, 0.599 mmol) at 0 °C successively, and stirred at this temperature for 15 min. The reaction was quenched with saturated aqueous NH_4Cl (5 mL), and the aqueous layer was extracted with Et_2O (5 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=50/1) to afford saturated ester **17b** (241.3 mg, 96%) as a colorless oil; R_f 0.29 (hexane/ethyl acetate=30/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65–7.63 (4H, m), 7.42–7.24 (6H, m), 5.67 (2H, ddd, *J*=10.4, 3.4, 3.4 Hz), 5.17 (2H, ddd, *J*=10.4, 2.0, 2.0 Hz), 4.07 (2H, q, *J*=7.1 Hz), 3.61 (2H, t, *J*=7.6 Hz), 2.46–2.45 (2H, m), 2.15 (2H, t, *J*=8.2 Hz), 1.64 (2H, t, *J*=7.6 Hz), 1.59 (2H, t, *J*=8.2 Hz), 1.21 (3H, t, *J*=7.1 Hz), 1.02 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.3, 135.6, 134.1, 129.4, 127.5, 125.4, 61.3, 60.1, 44.5, 38.5, 36.7, 30.1, 26.8, 26.3, 19.1, 14.2; IR (neat) ν_{max} 2931, 3858, 1736, 1589, 1113, 1086, 823, 737, 702 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{29}H_{39}O_3Si$: 463.2668, found: 463.2660.

*4.2.8. 4-(1-(2-(tert-Butyldiphenylsilyloxy)ethyl)cyclohexa-2,5-dienyl)-1-(phenylsulfonyl)butan-2-one (**17c**).* To a stirred solution of methyl phenyl sulfone (38.4 mg, 0.247 mmol) in THF (2 mL) was added *n*-BuLi (1.66 M in hexane, 0.296 mL, 0.494 mmol) at 0 °C and the solution was stirred at this temperature for 1 h. Then, to the reaction mixture was added a solution of **17b** (104 mg, 0.225 mmol) in THF (1 mL) via a cannula and the mixture was stirred at this temperature for 30 min. The reaction was quenched with saturated aqueous NH_4Cl (5 mL), and the aqueous layer was extracted with Et_2O (5 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=4/1) to afford saturated ester **17c** (121 mg, 95%) as a colorless oil; R_f 0.26 (hexane/ethyl acetate=4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87–7.85 (2H, m), 7.69–7.62 (5H, m), 7.58–7.54 (2H, m), 7.43–7.34 (6H, m), 5.68 (2H, ddd, *J*=10.2, 3.2, 3.2 Hz), 5.11 (2H, d, *J*=10.2 Hz), 4.09 (2H, s), 3.59 (2H, t, *J*=7.1 Hz), 2.50 (2H, t, *J*=7.8 Hz), 2.50–2.45 (2H, m), 1.61 (2H, t, *J*=7.8 Hz), 1.52 (2H, t, *J*=7.1 Hz), 1.01 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.7, 138.8, 135.6, 134.2, 134.0, 131.1, 129.5, 129.3, 128.3, 127.5, 125.6, 66.9, 61.3, 44,5, 40.4, 38.4, 34.9, 26.8, 19.1; IR (neat) ν_{max} 2931, 2856, 1720, 1587, 1524, 1155, 1111, 1085, 823, 742, 704 cm^{-1}; FAB HRMS $[M+Na]^+$ calcd for $C_{34}H_{40}O_4SiSNa$: 595.2314, found: 595.2291.

*4.2.9. 4-(1-(2-(tert-Butyldiphenylsilyloxy)ethyl)cyclohexa-2,5-diethyl)-1-diazo-1-phenylsulfonylbutan-2-one (**18**).* To a stirred solution of **17c** (85.9 mg, 0.150 mmol) in CH_3CN (1.5 mL) were added Et_3N (0.0818 mL, 0.300 mmol) and TsN_3 (45.6 mg, 0.450 mmol) successively at 0 °C, and the reaction mixture was stirred at this temperature over night. After the reaction was completed, CH_3CN was evaporated. Then, to the residue was added 2*N*-KOH (10 mL) and the aqueous layer was extracted with Et_2O (5 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=10/1) to afford diazo compound **18** (71.3 mg, 79%) as a pale yellow oil; R_f 0.49 (hexane/ethyl acetate=4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95–7.93 (2H, m), 7.67–7.61 (5H, m), 7.57–7.53 (2H, m), 7.42–7.33 (6H, m), 5.65 (2H, ddd, *J*=10.2, 3.2, 3.2 Hz), 5.08 (2H, ddd, *J*=10.2, 1.7, 1.7 Hz), 3.58 (2H, t, *J*=7.4 Hz), 2.47–2.43 (2H, m), 2.37 (2H, t, *J*=8.0 Hz), 1.59 (2H, t, *J*=7.4 Hz), 1.53 (2H, t, *J*=8.0 Hz), 1.01 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.8, 141.9, 135.5, 134.1, 134.0, 131.1, 129.5, 129.3, 127.5, 127.5, 125.5, 61.2, 44.5, 38.5, 35.3, 35.1, 26.8, 26.3, 19.1; IR (neat) ν_{max} 2931, 2856, 2106, 1666, 1589, 1344, 1155, 1111, 1086, 823, 756, 704 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{34}H_{39}O_4N_2SiS$: 599.2400, found: 599.2375.

*4.2.10. (1R,5S,6S,7R)-1-(2-(tert-Butyldiphenylsilyloxy)ethyl)-7-phenylsulfonyltricyclo[4.4.0.0^{5,7}]dec-2-ene-8-one (**12**).* To a stirred solution of toluene azeotroped $[CuOTf]_2PhMe$ (813 mg, 0.0945 mmol) in toluene (315 mL) was added a solution of toluene azeotroped ligand **6a** (1.23 g, 0.284 mmol) in toluene (5 mL) via a cannula, and the mixture was stirred at room temperature for 30 min. Then, to the solution was added toluene azeotroped **18** (18.9 g, 31.6 mmol) in toluene (5 mL) via a cannula, and the reaction mixture was stirred at this temperature for 11 h. The reaction was quenched with NH_4OH (3 mL) and H_2O (50 mL), and the aqueous layer was extracted with Et_2O (20 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=20/1) to afford **12** (12.9 g, 72%, 95% ee) as a colorless oil; R_f 0.38 (hexane/ethyl acetate=4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81–7.79 (2H, m), 7.68–7.62 (5H, m), 7.55–7.51 (2H, m), 7.45–7.39 (6H, m), 5.50 (1H, ddd, *J*=10.4, 3.4, 3.4 Hz), 5.05 (1H, d, *J*=10.4 Hz), 3.83–3.69 (2H, m), 2.62 (1H, d, *J*=9.8 Hz), 2.28–2.11 (3H, m), 2.07–1.98 (3H, m), 1.95–1.90 (1H, m), 1.82–1.76 (1H, m), 1.57–1.52 (1H, m), 1.07 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.4, 139.4, 135.6, 135.5, 133.7, 130.3, 129.7, 128.9, 128.8, 127.7, 127.7, 125.6, 60.8, 47.9, 44.1, 36.4, 35.9, 31.7, 28.4, 26.8, 22.5, 19.2, 19.1; IR (neat) ν_{max} 2929, 2858, 1707, 1589, 1307, 1149, 1113, 1088, 822, 756, 704 cm^{-1}; FAB HRMS $[M+Na]^+$ calcd for $C_{34}H_{38}O_4SiSNa$: 593.2158, found: 593.2166; $[\alpha]_D^{25}$ +71.3 (*c* 0.83, $CHCl_3$); Daicel CHIRALCEL OD-H 0.46φ×25 cm, hexane/isopropanol=9/1, flow rate=0.4 mL/min, retention time: 18.6 min for the minor, 22.2 min for the major.

*4.2.11. (1R,4aS,8R,8aR)-4,4a,8,8a-Tetrahydro-4a-(2-(tert-butyldiphenylsiloxy)ethyl)-1-(phenylsulfonyl)-8-(phenylthio)naphthalen-2(1H,3H,7H)-one (**19**).* To a stirred solution of PhSH (7.17 mL, 69.5 mmol) in THF (210 mL) was added *n*-BuLi (1.59 M in hexane, 42.3 mL, 67.3 mmol) at 0 °C, and the mixture was stirred at this temperature for 10 min. To the mixture was added a solution of **12** (12.8 g, 22.4 mmol) in THF (10 mL) at 0 °C via a cannula, the reaction mixture was refluxed for 9 h. The reaction was quenched with saturated aqueous NH_4Cl (30 mL) and the aqueous layer was extracted with Et_2O (20 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=20/1) to afford **19** (14.7 g, 96%) as a colorless oil; R_f 0.57 (benzene/ethyl acetate=40/1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90–7.86 (2H, m), 7.73–7.69 (3H, m), 7.67–7.64 (1H, m), 7.57–7.53 (2H, m), 7.44–7.36 (6H, m), 7.33–7.29 (2H, m), 7.29–7.22 (4H, m), 5.56 (1H, ddd, *J*=10.2, 5.1, 2.6 Hz), 5.47 (1H, d, *J*=10.2 Hz), 4.93 (1H, s), 3.95 (1H, ddd, *J*=10.5, 6.4, 6.4 Hz), 3.82 (1H, ddd, *J*=10.8, 6.4, 6.4 Hz), 3.14 (1H, d, *J*=10.8 Hz), 2.96 (1H, ddd, *J*=10.8, 9.7, 5.1 Hz), 2.85 (1H, ddd, *J*=16.4, 10.5, 5.6 Hz), 2.48 (1H, ddd, *J*=14.3, 6.4, 6.4 Hz), 2.39 (1H, ddd, *J*=17.7, 5.1, 5.1 Hz), 2.28 (1H, ddd, *J*=16.4, 5.8, 4.1 Hz), 2.22–2.15 (3H, m), 1.76 (1H, ddd, *J*=14.6, 10.5, 4.1 Hz), 1.06 (9H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 202.2, 146.8, 139.8, 135.7, 134.4, 133.9, 133.7, 133.6, 133.0, 129.5, 129.2, 129.1, 128.5, 127.8, 127.7, 127.6, 124.1, 74.7,

60.3, 49.1, 43.4, 41.0, 37.4, 36.3, 33.3, 32.1, 26.8, 19.1; IR (neat) ν_{max} 2929, 2856, 1712, 1585, 1309, 1147, 1111, 823, 754, 704 cm^{-1}; FAB HRMS $[M+Na]^+$ calcd for $C_{40}H_{44}O_4SiS_2Na$: 703.2348, found: 703.2354; $[\alpha]_D^{28}$ −17.7 (*c* 0.52, $CHCl_3$).

*4.2.12. (1R,4aS,8R,8aR)-1,2,3,4,4a,7,8,8a-Octahydro-4a-(2-(tert-butyldiphenylsiloxy)ethyl)-1-(phenylsulfonyl)-8-(phenylthio)naphthalen-2-ol (**19a**).* To a stirred solution of **19** (13.9 g, 20.4 mmol) in THF/MeOH (1/2) (210 mL) was added $NaBH_4$ (42.3 mL, 67.3 mmol) at 0 °C, and the reaction mixture was stirred at this temperature for 30 min. The reaction was quenched with saturated aqueous NH_4Cl (30 mL) and the aqueous layer was extracted with Et_2O (20 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=2/1) to afford **19a** (13.9 g, 100%) as a colorless oil; R_f 0.21 (hexane/ethyl acetate=4/1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.97–7.90 (2H, m), 7.75–7.67 (4H, m), 7.62–7.56 (1H, m), 7.55–7.47 (2H, m), 7.45–7.32 (8H, m), 7.30–7.22 (3H, m), 5.50 (1H, ddd, *J*=10.2, 4.3, 2.9 Hz), 5.43 (1H, d, *J*=10.2 Hz), 4.33 (1H, br), 3.93 (1H, ddd, *J*=10.2, 6.6, 6.6 Hz), 3.88–3.78 (2H, m), 3.74–3.66 (1H, m), 2.93 (1H, dd, *J*=8.2, 5.2 Hz), 2.50–2.34 (3H, m), 2.23 (1H, dddd, *J*=18.3, 7.3, 2.4, 2.4 Hz), 2.11–1.95 (2H, m), 1.88–1.80 (1H, m), 1.60–1.58 (1H, m), 1.44–1.34 (1H, m), 1.04 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.6, 135.7, 135.5, 134.1, 133.2, 131.9, 129.4, 129.1, 129.0, 127.8, 127.6, 127.5, 127.3, 123.0, 67.3, 67.1, 60.5, 45.3, 42.2, 42.0, 38.4, 32.7, 32.2, 28.0, 26.9, 19.1; IR (neat) ν_{max} 3513, 2929, 2858, 1585, 1304, 1140, 1082, 823, 754, 704 cm^{-1}; FAB HRMS $[M+Na]^+$ calcd for $C_{40}H_{46}O_4SiS_2Na$: 705.2505, found: 705.2514; $[\alpha]_D^{28}$ +11.7 (*c* 0.60, $CHCl_3$).

*4.2.13. (1R,4aS,8R,8aR)-1,2,3,4,4a,7,8,8a-Octahydro-4a-(2-(tert-butyldiphenylsiloxy)ethyl)-1-(phenylsulfonyl)-8-(phenylthio)naphthalen-2-ylmethanesulfonate (**19b**).* To a stirred solution of **19a** (14.5 g, 21.3 mmol) in 1,2-dichloro ethane (210 mL) were added Et_3N (14.8 mL, 0.107 mol) and MsCl (2.50 mL, 32.0 mmol), and the reaction mixture was stirred at 50 °C for 17 h. The reaction was quenched with saturated aqueous NH_4Cl (30 mL) and the aqueous layer was extracted with CH_2Cl_2 (20 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=20/1) to afford **19b** (15.8 g, 98%) as a colorless oil; R_f 0.21 (hexane/ethyl acetate=4/1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.96–7.91 (2H, m), 7.72–7.65 (4H, m), 7.63–7.57 (1H, m), 7.54–7.44 (2H, m), 7.44–7.23 (11H, m), 5.47–5.40 (2H, m), 3.95 (1H, ddd, *J*=10.2, 6.5, 6.5 Hz), 3.78 (1H, *J*=10.2, 6.6, 6.6 Hz), 3.40–3.32 (1H, m), 3.06 (1H, dd, *J*=9.6, 3.0 Hz), 2.72–2.60 (1H, m), 2.54–2.44 (1H, m), 2.36 (3H, s), 2.25–2.10 (2H, m), 2.05–1.95 (1H, m), 1.92–1.83 (1H, m), 1.74–1.70 (1H, m), 1.60–1.50 (2H, m), 1.04 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.2, 135.6, 135.2, 133.9, 133.8, 133.6, 133.2, 132.6, 129.4, 129.4, 129.1, 128.1, 127.8, 127.6, 127.5, 122.8, 64.4, 60.4, 60.3, 60.1, 45.8, 43.0, 38.0, 37.9, 26.8, 25.8, 21.0, 19.1, 14.2; IR (neat) ν_{max} 29,931, 2856, 1583, 1308, 1145, 1111, 823, 754, 704 cm^{-1}; FAB HRMS $[M-H]^+$ calcd for $C_{41}H_{47}O_6SiS_3$: 759.2304, found: 759.2328; $[\alpha]_D^{32}$ −9.6 (*c* 2.1, $CHCl_3$).

*4.2.14. (2-((1R,4aS,8aR)-1,2,4a,5,6,8a-Hexahydro-8-(phenylsulfonyl)-1-(phenylthio)naphthalen-4a-yl)ethoxy)(tert-butyl)diphenylsilane (**11**).* To a stirred solution of **19b** (141 mg, 0.186 mmol) in THF (2 mL) was added slowly a solution of *t*-BuOK (1.0 M in THF, 0.186 mL, 0.186 mmol) at −78 °C, and the reaction mixture was stirred at this temperature for 30 min. The reaction was quenched with saturated aqueous NH_4Cl (2 mL) and the aqueous layer was extracted with CH_2Cl_2 (5 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=20/1) to afford **11** (113.4 mg, 92%) as a colorless oil; R_f 0.42 (hexane/ethyl acetate=4/1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.79–7.74 (2H, m), 7.61–7.55 (4H, m), 7.46–7.31 (11H, m), 7.30–7.19 (3H, m), 7.10 (1H, dd, *J*=5.4, 2.7 Hz), 5.59 (1H, ddd, *J*=10.2, 3.7, 3.7 Hz), 5.37 (1H, d, *J*=10.2 Hz), 3.77 (1H, ddd, *J*=7.0, 7.0, 7.0 Hz), 3.56–3.44 (2H, m), 2.87 (1H, d, *J*=7.0), 2.29–2.17 (3H, m), 2.07–1.98 (1H, m), 1.65–1.53 (3H, m), 1.40–1.34 (1H, m), 1.00 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.6, 143.4, 141.4, 136.3, 135.5, 135.5, 134.0, 133.7, 133.6, 132.9, 131.8, 129.6, 129.0, 128.8, 127.7, 127.6, 126.8, 124.9, 59.9, 47.0, 42.3, 40.6, 38.8, 31.5, 30.4, 26.8, 23.3, 19.1; IR (neat) ν_{max} 2931, 2858, 1633, 1585, 1305, 1147, 1111, 823, 756, 704 cm^{-1}; FAB HRMS $[M+Na]^+$ calculated for $C_{40}H_{44}O_3SiS_2Na$: 687.2399, found: 687.2380; $[\alpha]_D^{31}$ −77.8 (*c* 1.4, $CHCl_3$).

*4.2.15. 2-((1R,4aS,8aR)-1,2,4a,5,6,8a-Hexahydro-8-(phenylsulfonyl)-1-(phenylthio)naphthalen-4a-yl)ethanol (**11a**).* To a stirred solution of **11** (469 mg, 0.705 mmol) in THF (7 mL) was added HF·Py (0.240 mL, 14.1 mmol) at room temperature, and the reaction mixture was stirred at the same temperature for 12 h. The reaction was quenched with saturated aqueous $NaHCO_3$ (2 mL) at 0 °C and the aqueous layer was extracted with Et_2O (5 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=10/1) to afford **11a** (263 mg, 87%) as a colorless oil; R_f 0.17 (hexane/ethyl acetate=1/1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.86–7.82 (2H, m), 7.59–7.54 (1H, m), 7.50–7.44 (2H, m), 7.43–7.38 (2H, m), 7.31–7.20 (3H, m), 7.14 (1H, dd, *J*=5.0, 2.8 Hz), 5.67 (1H, ddd, *J*=10.0, 3.7, 3.7 Hz), 5.44 (1H, d, *J*=10.0 Hz), 3.75 (1H, ddd, *J*=7.0, 7.0, 7.0 Hz), 3.54–3.42 (2H, m), 3.02 (1H, d, *J*=7.0), 2.40–2.17 (4H, m), 1.70–1.62 (1H, m), 1.60–1.53 (2H, m), 1.46–1.30 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4, 143.3, 141.1, 136.1, 134.2, 133.0, 131.6, 129.0, 128.9, 128.0, 126.8, 125.4, 58.9, 47.0, 41.3, 40.8, 39.0, 31.7, 31.3, 23.3; IR (neat) ν_{max} 3749, 2933, 2889, 1635, 1583, 1304, 1146, 1089, 752, 690 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{24}H_{27}O_3S_2$: 427.1402, found: 427.1418; $[\alpha]_D^{33}$ +115.2 (*c* 0.98, $CHCl_3$).

*4.2.16. 2-((1R,4aS,8aR)-1,2,4a,5,6,8a-Hexahydro-8-(phenylsulfonyl)-1-(phenylthio)naphthalen-4a-yl)acetaldehyde (**15**).* To a stirred solution of oxalyl chloride (0.0579 mL, 0.665 mmol) in CH_2Cl_2 (5 mL) was added DMSO (0.129 mL, 1.82 mmol) at −78 °C and the reaction solution was stirred at this temperature for 15 min. Then, to the mixture was added a solution of **11a** (258 mg, 0.605 mmol) in CH_2Cl_2 (2 mL) via a cannula. After stirred at −78 °C for 15 min, Et_3N (0.153 mL, 1.51 mmol) was added at the same temperature and the mixture was stirred at room temperature for 30 min. The resulting mixture was quenched with saturated aqueous brine (5 mL). The aqueous layer was extracted with CH_2Cl_2 (5 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=10/1) to afford aldehyde **15** (224 mg, 88%) as a whte solid; R_f 0.60 (hexane/ethyl acetate=1/1); ^1H NMR (400 MHz, $CDCl_3$) δ 9.49 (1H, t, *J*=2.0 Hz) 7.76–7.71 (2H, m), 7.60–7.54 (1H, m), 7.50–7.42 (4H, m), 7.37–7.25 (3H, m), 7.22 (1H, dd, *J*=6.2, 2.6 Hz), 5.81 (1H, ddd, *J*=10.2, 3.9, 3.9 Hz), 5.44 (1H, d, *J*=10.2 Hz), 4.09 (1H, ddd, *J*=5.3, 5.3, 5.3 Hz), 3.12 (1H, d, *J*=5.3 Hz), 2.71 (1H, dd, *J*=16.6, 2.0 Hz), 2.54 (1H, dd, *J*=16.6, 2.0 Hz), 2.39–2.30 (2H, m), 2.26–2.12 (2H, m), 1.66–1.52 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.9, 143.8, 142.7, 140.5, 135.4, 133.2, 131.8, 129.1, 129.0, 127.8, 127.1, 126.6, 52.2, 45.6, 41.4, 38.3, 31.7, 29.4, 22.9; IR (KBr) ν_{max} 2915, 2896, 2838, 1739, 1716, 1633, 1586, 1304, 1146, 739, 687 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{24}H_{25}O_3S_2$: 425.1245, found: 425.1251; mp 109–110 °C; $[\alpha]_D^{33}$ +119.5 (*c* 0.99, $CHCl_3$).

*4.2.17. (1S,6R,8R)-7-(Phenylsulfonyl)-5-(phenylthio)tricyclo[6.2.2.0^{1,6}]dodec-2-en-9-ol (**14**).* To a solution of **15** (4.68 g, 11.0 mmol) and MeOH (0.84 mL, 22.0 mmol) in degassed THF (1100 mL) was added a THF solution of SmI_2 (prepared with Sm

(11.6 g, 77.3 mmol) and 1,2-diiodoethane (10.5 g, 38.5 mmol)) in degassed THF (350 mL) at 0 °C until the color of the mixture turned to blue. Then, the reaction mixture was stirred at 0 °C for 1 h. The reaction was quenched with saturated aqueous NH_4Cl (200 mL) and the aqueous layer was extracted with Et_2O (200 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=5/1) to afford **14** (4.48 g, 95%) as a white solid; R_f 0.48 (hexane/ethyl acetate=1/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82–7.76 (2H, m), 7.45–7.39 (1H, m), 7.33–7.15 (7H, m), 5.53 (1H, ddd, *J*=9.8, 5.1, 2.9 Hz), 5.29 (1H, d, *J*=9.8 Hz), 4.48 (1H, ddd, *J*=9.5, 3.8, 1.0 Hz), 4.24 (1H, ddd, *J*=11.7, 8.8, 6.1 Hz), 4.18 (1H, dd, *J*=8.5, 5.1 Hz), 2.68–2.65 (1H, m), 2.55–2.42 (3H, m), 2.19–2.07 (2H, m), 1.91 (2H, dd, *J*=13.9, 8.5 Hz), 1.79 (1H, br), 1.36–1.22 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6, 134.5, 133.4, 132.2, 130.5, 128.7, 128.3, 126.3, 126.2, 123.3, 68.5, 61.4, 44.8, 44.6, 39.1, 35.1, 33.3, 26.5, 20.1; IR (KBr) ν_{max} 3465, 2918, 2876, 1735, 1583, 1300, 1283, 1136, 728, 688 cm^{-1}; FAB HRMS $[M]^+$ calcd for $C_{24}H_{26}O_3S_2$: 426.1323, found: 426.1338; mp 61–65 °C; $[\alpha]_D^{34}$ −26.5 (*c* 0.99, $CHCl_3$).

*4.2.18. (1R,6R,8S)-Tricyclo[6.2.2.0^{1,6}]dodec-2-en-9-ol (**20**).* To a stirred solution of **14** (191.3 mg, 0.448 mmol) in THF (4.5 mL) was added a solution of lithium napthalenide (prepared with Li dispersion (30%) (311 mg, 13.5 mmol) and naphthalene (1.72 g, 13.5 mmol) in THF (30 mL)) at −78 °C until the color of the mixture turned to dark green. After stirred at −78 °C for 1 h, the reaction mixture was stirred at −20 °C for 1 h. The reaction was quenched with saturated aqueous NH_4Cl (10 mL) and the aqueous layer was extracted with Et_2O (5 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=100/1) to afford **20** (55.1 mg, 69%) as a white solid; R_f 0.48 (hexane/ethyl acetate=1/1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.56 (1H, ddd, *J*=10.0, 2.8, 1.5 Hz), 5.24 (1H, ddd, *J*=10.0, 2.3, 2.3 Hz), 4.02 (1H, dd, *J*=10.0, 9.0, 4.4 Hz), 2.13–2.08 (1H, m), 2.05–1.94 (2H, m), 1.88 (1H, dd, *J*=14.0, 8.8 Hz), 1.75–1.69 (2H, m), 1.62–1.56 (2H, m), 1.53–1.48 (1H, m), 1.45–1.40 (1H, m), 1.36–1.31 (1H, m), 1.18–1.15 (1H, m), 1.09 (1H, dddd, *J*=13.1, 11.3, 2.0, 2.0 Hz), 0.92 (1H, dd, *J*=13.7, 8.7 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 134.7, 125.9, 70.2, 45.1, 35.3, 32.7, 31.6, 27.8, 26.2, 26.1, 25.7, 24.3; IR (KBr) ν_{max} 3314, 2917, 2858, 1646, 103, 700 cm^{-1}; FAB HRMS $[M-OH]^+$ calcd for $C_{12}H_{17}$: 161.1330, found: 161.1323; mp 65–67 °C; $[\alpha]_D^{34}$ −171.0 (*c* 0.49, $CHCl_3$).

*4.2.19. (1R,6S,8S)-Tricyclo[6.2.2.0^{1,6}]dodec-2-ene-4,9-diol (**21**).* To a stirred solution of **20** (42.1 mg, 23.6 mmol) in 1,4-dioxane (3 mL) was added SeO_2 (78.6 mg, 70.8 mmol). The mixture was refluxed for 1.5 h. The reaction was quenched with saturated aqueous $NaHCO_3$ (5 mL) and the aqueous layer was extracted with Et_2O (5 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=1/1) to afford **21** (45.8 mg, 100%) as a colorless oil; R_f 0.16 (hexane/ethyl acetate=1/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.73 (1H, ddd, *J*=9.8, 4.9, 1.5 Hz), 5.46 (1H, d, *J*=9.8 Hz), 4.09 (1H, ddd, *J*=4.9, 4.9, 1.5 Hz), 4.04 (1H, dd, *J*=9.0, 4.3 Hz), 2.19–2.12 (1H, m), 2.03–1.95 (1H, m), 1.90 (1H, dd, *J*=13.9, 9.0 Hz), 1.81–1.73 (2H, m), 1.64 (1H, dd, *J*=13.9, 4.4 Hz), 1.48–1.30 (3H, m), 1.25–1.19 (1H, m), 1.12–1.04 (1H, m), 0.96–0.89 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.1, 126.7, 69.6, 64.3, 44.4, 35.1, 33.2, 31.5, 29.3, 27.3, 24.1, 23.9; IR (neat) ν_{max} 3400, 2933, 2861, 1647, 1441, 1024, 756 cm^{-1}; FAB HRMS $[M-OH]^+$ calcd for $C_{12}H_{17}O$: 177.1279, found: 177.1285; $[\alpha]_D^{24}$ −178.8 (*c* 0.62, $CHCl_3$).

*4.2.20. (1R,6S,8S)-4-(tert-Butyldimethylsiloxy)tricyclo[6.2.2.0^{1,6}]dodec-2-ene-9-ol (**13**).* To a stirred solution of **21** (10.9 mg, 0.0561 mmol) in DMF (1 mL) were added imidazole (11.5 mg, 0.168 mmol) and TBSCl (33.9 mg, 0.225 mmol), and the mixture was stirred at −20 °C for 2 h. The reaction was quenched with saturated aqueous NH_4Cl (5 mL) and the aqueous layer was extracted with Et_2O (5 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=100/1) to afford silyl ether **13** (11.9 mg, 69%) as a white solid and bis silyl ether **13′** (4.74 mg, 20%). Bis silyl ether **13′** was converted to **21** (TBAF, THF, 84%) and reused; R_f 0.40 (hexane/ethyl acetate=4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.57 (1H, ddd, *J*=9.8, 4.9, 1.0 Hz), 5.36 (1H, d, *J*=9.8 Hz), 4.10–4.08 (1H, m), 4.02 (1H, dd, *J*=9.0, 4.1 Hz), 2.16–2.01 (2H, m), 1.88 (1H, dd, *J*=13.9, 9.0 Hz), 1.78–1.73 (1H, m), 1.63–1.50 (4H, m), 1.45–1.30 (2H, m), 1.27–1.21 (1H, m), 1.09–1.01 (1H, m), 0.89 (9H, s), 0.06 (3H, s), 0.05 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.3, 127.6, 69.8, 64.6, 44.7, 36.0, 33.0, 31.6, 29.2, 27.4, 26.0, 24.3, 24.1, 18.3, −4.4, −4.6; IR (KBr) ν_{max} 3301, 2936, 2857, 1648, 1471, 1250, 1051, 1032, 833 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{18}H_{31}O_2Si$: 307.2093, found: 307.2096; mp 108–111 °C; $[\alpha]_D^{25}$ −159.5 (*c* 0.39, $CHCl_3$).

*4.2.21. (1R,6S,8S)-4-(tert-Butyldimethylsiloxy)tricyclo[6.2.2.0^{1,6}]dodec-2-en-9-one (**13a**).* To a stirred solution of **13** (510 mg, 1.65 mmol) in CH_2Cl_2 (20 mL) was added Dess–Martin periodinane (3.51 g, 8.27 mmol) and the mixture was stirred at room temperature for 30 min. The reaction was quenched with saturated aqueous $NaHCO_3$ (5 mL) and saturated aqueous $Na_2S_2O_3$ (5 mL). The aqueous layer was extracted with Et_2O (5 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=1/1) to afford **13a** (482 mg, 95%) as a colorless oil; R_f 0.67 (hexane/ethyl acetate=4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.56 (1H, dd, *J*=10.0, 4.9 Hz), 5.47 (1H, d, *J*=10.0 Hz), 4.18–4.14 (1H, m), 2.32–2.25 (2H, m), 2.12–1.96 (3H, m), 1.80–1.61 (5H, m), 1.46–1.37 (1H, m), 1.28–1.21 (1H, m), 0.88 (9H, s), 0.07 (3H, s), 0.06 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 216.4, 135.2, 128.3, 64.5, 50.0, 43.0, 36.3, 35.5, 31.1, 30.5, 25.9, 24.3, 24.0, 18.2, −4.4, −4.7; IR (neat) ν_{max} 2951, 2858, 1728, 1471, 1254, 1254, 1055, 835 cm^{-1}; FAB HRMS $[M-H]^+$ calcd for $C_{18}H_{29}O_2Si$: 305.1937, found: 305.1939; $[\alpha]_D^{26}$ −114.6 (*c* 1.1, $CHCl_3$).

*4.2.22. (1R,8S)-4-(tert-Butyldimethylsiloxy)-9-methylidenetricyclo[6.2.2.0^{1,6}]dodec-2-ene(**22**).* To a stirred solution of toluene azeotroped methyl triphenylphosphomiumbromide (2.02 g, 5.65 mmol) in THF (12 mL) was added *n*-BuLi (1.66 M in hexane, 3.07 mL, 5.09 mmol) at 0 °C and the mixture was stirred at this temperature for 10 min. Then, a toluene azeotroped **13a** (347 mg, 1.13 mmol) was added at 0 °C, and the reaction mixture was stirred at 50 °C for 1.5 h. The reaction was quenched with saturated aqueous NH_4Cl (5 mL) and the aqueous layer was extracted with Et_2O (5 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by short column chromatography (hexane only) to afford crude silyl ether **22** and this was used for the next step without further purification.

*4.2.23. (1R,6S,8S)-9-Methylidenetricyclo[6.2.2.0^{1,6}]dodec-2-en-4-ol (**22a**).* To a stirred solution of crude **22** in THF (12 mL) was added TBAF (1.0 M in THF, 9.04 mL, 9.04 mmol), and the solution was stirred at 60 °C for 1 h. The reaction was quenched with saturated aqueous NH_4Cl (5 mL), and the aqueous layer was extracted with Et_2O (5 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=20/1) to afford **22a** (205 mg, 95% (two steps)) as a colorless oil; R_f 0.41 (hexane/ethyl acetate=4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.73 (1H, ddd, *J*=9.8, 4.9, 1.2 Hz), 5.54 (1H, d, *J*=9.8 Hz), 4.78 (1H, d, *J*=2.4 Hz), 4.63 (1H, d, *J*=2.4 Hz), 4.13–4.12 (1H, m), 2.30 (1H, dt, *J*=16.3, 2.7 Hz), 2.23 (1H, br), 2.07–2.02 (1H, m), 1.94–1.87 (1H, m), 1.85–1.73 (2H, m), 1.67

(1H, dd, *J*=13.4, 4.1 Hz), 1.64–1.49 (3H, m), 1.32–1.25 (1H, m), 1.11 (1H, ddd, *J*=12.2, 8.0, 1.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.1, 139.3, 126.5, 105.8, 64.4, 41.6, 35.9, 34.9, 34.7, 34.5, 30.6, 26.7, 25.3; IR (neat) ν_{max} 3324, 2933, 2862, 1646, 1429, 1167, 1045, 1001, 875, 756 cm^{-1}; FAB HRMS $[M-H]^+$ calcd for $C_{13}H_{17}O$: 189.1279, found: 189.1278; $[\alpha]_D^{27}$ −163.2 (*c* 1.1, $CHCl_3$).

*4.2.24. (1R,6S,8S)-9-Methylidenetricyclo[6.2.2.0^{1,6}]dodec-2-en-4-one (**4**).* To a stirred solution of **22a** (20.3 mg, 0.107 mmol) in CH_2Cl_2 (1 mL) were added $NaHCO_3$ (86.0 mg, 1.07 mmol) and Dess–Martin periodinane (226 mg, 0.530 mmol), and the mixture was stirred at room temperature for 1 h. The reaction was quenched with saturated aqueous $NaHCO_3$ (5 mL) and saturated aqueous $Na_2S_2O_3$ (5 mL). The aqueous layer was extracted with Et_2O (5 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=4/1) to afford **4** (16.4 mg, 82%) as a colorless oil; R_f 0.56 (hexane/ethyl acetate=4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.57 (1H, d, *J*=10.0 Hz), 5.88 (1H, d, *J*=10.0 Hz), 4.83 (1H, d, *J*=1.7 Hz), 4.69 (1H, d, *J*=1.7 Hz), 2.48–2.40 (2H, m), 2.36–2.29 (2H, m), 2.19–2.08 (2H, m), 2.03–1.96 (1H, m), 1.82–1.68 (3H, m), 1.55–1.48 (1H, m), 1.20 (1H, ddd, *J*=12.6, 7.8, 1.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.1, 156.7, 148.9, 127.7, 106.9, 41.6, 40.8, 36.0, 35.5, 35.4, 34.8, 26.3, 24.5; IR (neat) ν_{max} 2939, 2866, 1684, 1429, 1273, 1236, 1167, 877, 765 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{13}H_{17}O$: 189.1279, found: 189.1288; $[\alpha]_D^{25}$ +21.2 (*c* 0.1, $CHCl_3$) (lit.[4f] $[\alpha]_D^{25}$ +21.2 (*c* 1.0, $CHCl_3$)).

*4.2.25. tert-Butyldiphenyl(2-((3aS,7R,7aR)-7b-(phenylperoxythio)-7-(phenylthio)-1a,2,3,3a,6,7,7a,7b-octahydronaphtho[2,1-b]oxiren-3a-yl)ethoxy)silane (**23**).* To a stirred solution of TBHP (2.38 mL, 13.1 mmol) in THF (75 mL) was added a solution of *n*-BuLi (1.65 M in hexane, 7.45 mL, 12.2 mmol) dropwise at −78 °C, and the reaction mixture was stirred at this temperature for 15 min. Then, to the reaction mixture was added a solution of **11** (5.45 g, 8.19 mmol) in THF (5 mL) via a cannula at −78 °C, and the mixture was stirred at 40 °C for 30 min. The resulting mixture was quenched with brine (20 mL). The aqueous layer was extracted with Et_2O (10 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=20/1) to afford epoxide **23** (5.58 g, 100%) as a colorless solid as a colorless oil; R_f=0.31 (hexane/ethyl acetate=4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02–7.98 (2H, m), 7.71–7.66 (4H, m), 7.65–7.60 (1H, m), 7.54–7.49 (2H, m), 7.48–7.37 (8H, m), 7.29–7.18 (3H, m), 5.43 (1H, ddd, *J*=10.0, 5.4, 2.2 Hz), 5.38 (1H, d, *J*=10.0 Hz), 3,82 (1H, ddd, *J*=13.7, 7.8, 7.0 Hz), 3.65 (1H, ddd, *J*=13.7, 7.1, 7.1 Hz), 3.56–3.52 (1H, m), 3.12 (1H, ddd, *J*=11.0, 11.0, 5.4 Hz), 2.87 (1H, d, *J*=11.0 Hz), 2.36 (1H, ddd, *J*=17.8, 5.4, 5.4 Hz), 2.28 (1H, ddd, *J*=17.8, 11.0, 2.2 Hz), 1.91 (1H, dd, *J*=16.3, 5.36 Hz), 1.83–1.74 (2H, m), 1.66–1.53 (1H, m), 1.30 (1H, ddd, *J*=19.3, 14.1, 5.6 Hz), 1.17–1.10 (1H, m), 1.05 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.3, 135.7, 135.6, 134.2, 133.6, 133.5, 133.1, 132.7, 130.3, 129.6, 129.6, 128.8, 128.8, 127.7, 127.7, 127.1, 124.2, 74.9, 59.9, 56.7, 44.3, 39.9, 38.4, 37.4, 35.0, 26.8, 26.0, 20.0, 19.1; IR (neat) ν_{max} 2931, 2857, 1585, 1473, 1427, 1216, 1153, 1110, 823, 757, 703 cm^{-1}; FAB HRMS $[M+Na]^+$ calcd for $C_{40}H_{44}O_4SiS_2Na$: 703.2348, found: 703.2327; $[\alpha]_D^{27}$ +47.3 (*c* 0.78, $CHCl_3$).

*4.2.26. (4aS,8R,8aS)-4a-2-(tert-Butyldiphenylsilyloxyethyl)-8-phenylthio-2,3,4,4a,8,8a-hexahydronaphthalen-1(7H)-one (**25**).* To a stirred suspension of dry Mg turnings (14.7 mg, 6.03 mmol) in anhydrous Et_2O (10 mL) was added 1,2-diiodoethane (197.4 mg, 7.24 mmol) and the solution was stirred at room temperature for 20 min (disappearance of Mg was observed). To neat **23** (80.2 mg, 0.121 mmol) was added this reaction mixture via a cannula and the mixture was stirred at room temperature for 24 h. The resulting mixture was quenched with a mixture of saturated aqueous $NaHCO_3$ (5 mL) and saturated aqueous $Na_2S_2O_3$ (5 mL). The aqueous layer was extracted with Et_2O (10 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=10/1) to afford ketone **25** (53.7 mg, 82%) as a colorless oil; R_f=0.52 (hexane/ethyl acetate=4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65–7.63 (2H, m), 7.48–7.46 (4H, m), 7.45–7.34 (6H, m), 7.31–7.27 (3H, m), 5.49–5.47 (2H, m), 3.71 (1H, ddd, *J*=10.2, 7.8, 6.1 Hz), 3.60 (1H, ddd, *J*=10.2, 7.3, 6.1 Hz), 3.53 (1H, ddd, *J*=12.0, 11.2, 5.4 Hz), 2.44–2.34 (3H, m), 2.30–2.23 (1H, m), 2.02 (1H, dd, *J*=17.6, 11.2 Hz), 1.88–1.80 (1H, m), 1.80–1.66 (3H, m), 1.64–1.54 (2H, m), 1.01 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.1, 135.6, 135.5, 134.3, 134.2, 133.6, 133.6, 132.5, 129.6, 128.9, 127.9, 127.7, 127.6, 124.0, 60.1, 59.8, 44.1, 43.1, 39.1, 38.6, 33.5, 33.0, 26.8, 22.3, 19.0; IR (neat) ν_{max} 2929, 2856, 1708, 1587, 1473, 1427, 823, 752, 701 cm^{-1}; FAB HRMS $[M+Na]^+$ calcd for $C_{34}H_{40}O_2SiSNa$: 563.2416, found: 563.2403; $[\alpha]_D^{28}$ +41.5 (*c* 0.70, $CHCl_3$).

*4.2.27. (4aS,8aS)-4a-2-(tert-Butyldiphenylsilyloxyethyl)-2,3,4,4a,8,8a-hexahydronaphthalen-1(7H)-one (**25a**).* To a stirred solution of **25** (4.3 g, 7.88 mmol) in MeOH/THF (2/1) (100 mL) was added a excess amount of Raney-Ni under an atmosphere of Ar, and the reaction mixture was stirred at room temperature for 6 h. After the reaction was completed, to the reaction mixture was added acetone (100 mL) and stirred over night. Then the mixture was filtered through a plug of Celite, and the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane/ethyl acetate=10/1) to afford ketone **25a** (3.4 g, 84%) as a colorless oil; R_f=0.52 (benzene/ethyl acetate=40/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67–7.64 (4H, m), 7.45–7.36 (6H, m), 5.60 (1H, ddd, *J*=10.2, 3.4, 3.4 Hz), 5.54 (1H, ddd, *J*=10.2, 2.2, 2.2 Hz), 3.74 (2H, dd, *J*=7.1, 7.1 Hz), 2.38–2.27 (2H, m), 2.20–2.00 (3H, m), 1.93–1.83 (1H, m), 1.79–1.59 (1H, m), 1.03 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.9, 135.6, 135.5, 133.7, 133.7, 133.6, 129.6, 127.6, 127.5, 60.2, 52.5, 43.1, 40.3, 40.3, 34.4, 26.8, 22.6, 21.7, 19.9, 19.0; IR (neat) ν_{max} 2931, 2856, 1707, 1589, 1471, 1427, 1110, 823, 701 cm^{-1}; FAB HRMS $[M+Na]^+$ calcd for $C_{28}H_{36}O_2SiNa$: 455.2382, found: 455.2392; $[\alpha]_D^{29}$ +62.5 (*c* 0.40, $CHCl_3$).

*4.2.28. (4aS,8aS)-4a-(2-Hydroxyethyl)-2,3,4,4a,8,8a-hexahydronaphthalen-1(7H)-one (**26**).* To a stirred solution of **25a** (510 mg, 1.18 mmol) in THF (12 mL) was added a solution of tetra-*n*-butylammonium fluoride (1.0 M in THF, 1.8 mL, 1.77 mmol), and the reaction mixture was stirred at 50 °C for 30 min. The resulting mixture was quenched with saturated aqueous NH_4Cl (2 mL). The aqueous layer was extracted with Et_2O (5 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=2/1) to afford alcohol **26** (210 mg, 92%) as a colorless oil; R_f=0.11 (hexane/ethyl acetate=1/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.71 (1H, ddd, *J*=10.2, 3.7, 3.7 Hz), 5.46 (1H, ddd, *J*=10.2, 2.2, 2.2 Hz), 3.75 (2H, dd, *J*=7.3, 7.3 Hz), 2.45–2.36 (1H, m), 2.34–2.31 (1H, m), 2.29–2.04 (3H, m), 2.00–1.91 (1H, m), 1.88–1.79 (3H, m), 1.77–1.60 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.0, 133.4, 128.1, 59.2, 52.8, 43.5, 40.4, 40.0, 34.7, 22.8, 21.7, 20.3; IR (neat) ν_{max} 3419, 2937, 2869, 1558, 1051 cm^{-1}; FAB HRMS $[M+Na]^+$ calcd for $C_{12}H_{18}O_2Na$: 217.1204, found: 217.1206; $[\alpha]_D^{27}$ +90.4 (*c* 0.34, $CHCl_3$).

*4.2.29. 2-((4aS,8aS)-1-Oxo-1,2,3,4,4a,7,8,8a-octahydronaphthalen-4a-yl)acetaldehyde (**26a**).* To a stirred solution of oxalyl chloride (0.330 mL, 3.76 mmol) in CH_2Cl_2 (20 mL) at −78 °C was added DMSO (0.534 mL, 7.53 mmol) and the reaction solution was stirred at this temperature for 15 min. Then, to the mixture was added a solution of **26** (487 mg, 2.51 mmol) in CH_2Cl_2 (5 mL). After stirred at −78 °C for 30 min, Et_3N (0.874 mL, 6.27 mmol) was added and

the mixture was stirred at room temperature for 30 min. The resulting mixture was quenched with saturated aqueous brine (5 mL). The aqueous layer was extracted with CH_2Cl_2 (5 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=20/1) to afford aldehyde **26a** (438 mg, 91%) as a colorless oil; R_f=0.36 (hexane/ethyl acetate=1/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (1H, dd, J=2.9, 2.4 Hz), 5.80 (1H, ddd, J=10.2, 3.4, 3.4 Hz), 5.53 (1H, ddd, J=10.2, 2.2, 2.2 Hz), 2.63 (1H, dd, J=15.4, 2.4 Hz), 2.46 (1H, dd, J=15.4, 2.9 Hz), 2.47–2.38 (2H, m), 2.31–2.14 (3H, m), 2.04–1.62 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.0, 201.8, 131.7, 129.7, 54.4, 52.2, 40.7, 40.4, 35.2, 22.2, 21.6, 19.4; IR (neat) ν_{max} 2938, 2867, 2732, 1716, 1708, 1455, 1170 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for r $C_{12}H_{17}O_2$: 193.1229, found: 193.1229; $[\alpha]_D^{26}$ +118.3 (*c* 0.49, $CHCl_3$).

*4.2.30. (4aS,8aS)-4a-(3-Methoxyallyl)-2,3,4,4a,8,8a-hexahydronaphthalen-1(7H)-one (**27**).* To a stirred suspension of toluene azeotroped (methoxymethyl)triphenyl phosphonium chloride (83.0 mg, 0.242 mmol) in THF (1 mL) was added NaHMDS (1.07 M in THF, 0.181 mL, 0.193 mmol) at 0 °C and the mixture was stirred at this temperature for 1 h min. Then, to the reaction solution was added a solution of **26a** (30.1 mg, 0.161 mmol) in THF (0.5 mL) via a cannula. After stirred at −78 °C for 10 min, cooling bath was removed and the mixture was stirred for 10 min. The resulting solution was quenched with saturated aqueous NH_4Cl (2 mL). The aqueous layer was extracted with Et_2O (5 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=50/1) to afford methyl enol ether **27** (32.1 mg, 90%, *E*/*Z*=1/2 mixture) as a colorless oil; R_f=0.47 (hexane/ethyl acetate=4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.27 (0.5H, d, J=12.7 Hz), 6.01 (1H, d, J=6.6 Hz), 5.67 (1.5H, ddd, J=10.2, 3.4, 3.4 Hz), 5.42–5.38 (1.5H, m), 4.70 (0.5H, ddd, J=12.7, 7.8, 7.8 Hz), 4.35 (1H, ddd, J=6.6, 6.6, 6.6 Hz), 3.57 (3H, s), 3.53 (3H, s), 2.47–1.66 (19.5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.7, 213.4, 149.3, 148.2, 134.1, 133.9, 127.7, 127.5, 101.5, 97.5 59.5, 56.1, 51.7, 51.6, 41.7, 41.5, 40.4, 40.3, 38.9, 34.8, 33.7, 33.7, 22.8, 22.7, 21.6, 21.6, 20.0, 19.8; IR (neat) ν_{max} 2935, 2856, 1705, 1662, 1652, 1455, 1209, 1106 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{14}H_{21}O_2$: 221.1542, found: 221.1544; $[\alpha]_D^{27}$ +120.6 (*c* 0.90, $CHCl_3$).

*4.2.31. ((4aS,8aS)-4a-(3-Methoxyallyl)-3,4,4a,7,8,8a-hexahydronaphthalen-1-yloxy)trimethylsilane (**27a**).* To a stirred solution of diisopropylamine (0.0343 mL, 0.245 mmol) in THF (1 mL) was added a solution of *n*-BuLi (1.57 M in hexane, 0.151 mL, 0.270 mmol) at 0 °C, and the reaction solution was stirred at this temperature for 15 min. Then, to the reaction mixture was added a solution of **27** (17.4 mg, 0.0790 mmol) in THF (1 mL) via a cannula, and the mixture was stirred at 0 °C for 30 min. After Et_3N (0.0330 mL, 0.270 mmol) and TMSCl (0.0302 mL, 0.270 mmol) were added, the solution was stirred 0 °C for 10 min. The resulting mixture was quenched with saturated aqueous NH_4Cl (2 mL). The aqueous layer was extracted with Et_2O (5 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The crude silyl enol ether **27a** was used for the next step without further purification.

*4.2.32. (4aS,8aS)-4a-(3-Methoxyallyl)-4,4a,8,8a-tetrahydronaphthalen-1(7H)-one (**10**).* 4-Methoxypyridine-*N*-oxide (MPO) (44.0 mg, 0.158 mmol) and IBX (19.8 mg, 0.158 mmol) were added to DMSO (0.1 mL) and the resulting mixture was stirred at room temperature for 30 min (disappearance of MPO and IBX was observed and the mixture turned to clear solution.). Then, to a neat **27a** was added the MPO-IBX complex solution in DMSO (0.2 mL) via a cannula and the solution was stirred at room temperature for 2 h. The resulting mixture was quenched with saturated aqueous $NaHCO_3$ (1 mL). The aqueous layer was extracted with Et_2O (5 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=20/1) to afford enone **10** (12.0 mg, 70% (two steps), *E*/*Z*=1/2 mixture) as a colorless oil; R_f=0.58 (hexane/ethyl acetate=2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.80 (1.5H, ddd, J=10.2, 4.1, 4.1 Hz), 6.21 (1H, d, J=12.4 Hz), 6.04–5.96 (2.5H, m), 5.75–5.66 (1.5H, m), 5.49 (1.5H, ddd, J=10.4, 2.2, 2.2 Hz), 4.63 (0.5H, ddd, J=12.7, 7.8, 7.8 Hz), 4.29 (1H, ddd, J=7.8, 7.8, 7.8 Hz), 3.54 (3H, s), 3.51 (1.5H, s), 2.44–2.27 (5H, m), 2.19–2.03 (5H, m), 1.97–1.73 (3.5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2, 202.1, 149.4, 148.4, 147.3, 147.1, 134.0, 133.5, 128.7, 128.5, 127.4, 127.3, 101.3, 97.4, 59.4, 56.1, 49.8, 49.5, 39.8, 39.7, 37.4, 35.5, 35.2, 33.3, 24.0, 21.7; IR (neat) ν_{max} 2933, 2838, 1668, 1455, 1388, 1211, 1106, 937 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{14}H_{19}O_2$: 219.1385, found: 219.1394; $[\alpha]_D^{25}$ +129.5 (*c* 0.60, $CHCl_3$).

*4.2.33. (1S,9S,10S)-7-Oxotricyclo[7.2.1.0^{1,6}]dodec-2-ene-10-carbaldehyde (**9**).* To a stirred solution of **10** (2.0 mg, 9.14×10^{-3} mmol) in acetone (0.1 mL) and toluene (1 mL) was added PTSA·H_2O (5.2 mg, 2.74×10^{-2} mmol) and the mixture was stirred at room temperature for 1.5 days. The reaction was quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with Et_2O (2 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=20/1) to afford aldehyde **9** (1.8 mg, 96%) as a white solid; R_f=0.47 (hexane/ethyl acetate=2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.65 (1H, d, J=1.0 Hz), 5.72 (1H, ddd, J=10.2, 3.4, 3.4 Hz), 5.46 (1H, d, J=10.2 Hz), 2.77 (1H, dd, J=8.0, 4.4 Hz), 2.73–2.65 (1H, m), 2.52 (1H, dd, J=17.3, 3.7 Hz), 2.47–2.38 (1H, m), 2.34–2.24 (1H, m), 2.15–2.07 (2H, m), 2.00 (1H, dd, J=13.9, 6.3 Hz), 1.84–1.48 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 214.2, 200.8, 132.7, 128.0, 57.8, 55.0, 47.6, 45.3, 39.1, 38.2, 35.0, 25.4, 24.9; IR (neat) ν_{max} 2940, 2869, 2717, 1720, 1704, 1454, 1224, 756, 705 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{13}H_{17}O_2$: 205.1229, found: 205.1229; $[\alpha]_D^{24}$ +41.3 (*c* 0.30, $CHCl_3$); mp 75.7–77.3 °C.

*4.2.34. (1S,9S,10S)-10-(Hydroxymethyl)tricyclo[7.2.1.0^{1,6}]dodec-2-en-7-one (**9a**).* To a suspension of $NaBH_4$ (7.5 mg, 0.198 mmol) in EtOH/CH_2Cl_2 (1/3) (1 mL) at −78 °C was added a solution of **9** (2.7 mg, 1.32×10^{-2} mmol) in EtOH/CH_2Cl_2 (1/3) (0.5 mL) and the mixture was stirred this temperature for 1.5 h. The reaction was quenched with saturated aqueous NH_4Cl (2 mL). The aqueous layer was extracted with Et_2O (2 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=2/1) to afford alcohol **9a** (2.5 mg, 93%) as a colorless oil; R_f=0.14 (hexane/ethyl acetate=2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.70 (1H, ddd, J=10.2, 3.7, 3.7 Hz), 5.44 (1H, ddd, J=10.2, 2.0, 2.0 Hz), 3.51 (1H, dd, J=10.5, 6.1 Hz), 3.45 (1H, dd, J=10.4, 8.0 Hz), 2.47 (1H, dd, J=16.8, 3.9 Hz), 2.43–2.39 (1H, m), 2.38–2.32 (1H, m), 2.29–2.22 (1H, m), 2.17–2.07 (2H, m), 2.05–1.95 (1H, m), 1.84–1.75 (2H, m), 1.75–1.64 (4H, m), 1.25 (1H, dd, J=13.4, 6.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 215.9, 133.6, 127.3, 66.6, 57.6, 48.5, 45.4, 45.1, 42.6, 38.8, 36.4, 25.5, 24.9; IR (neat) ν_{max} 3386, 2939, 2865, 1670, 1452, 1228 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{13}H_{19}O_2$: 207.1385, found: 207.1382; $[\alpha]_D^{25}$ +74.0 (*c* 0.73, $CHCl_3$).

*4.2.35. (1S,9S,10S)-10-(Iodomethyl)tricyclo[7.2.1.0^{1,6}]dodec-2-en-7-one (**9b**).* To a stirred solution of **9a** (47.4 mg, 0.230 mmol) in benzene (2.5 mL) were added imidazole (62.5 mg, 0.919 mmol), triphenylphospine (129.7 mg, 0.460 mmol), and I_2 (116.6 mg, 0.460 mmol) at room temperature, and the solution was stirred at this temperature for 2 h. The reaction was quenched with a mixture of saturated aqueous $NaHCO_3$ (1 mL) and saturated aqueous Na_2SO_3 (1 mL). The aqueous layer was extracted with Et_2O (5 mL×2). The

combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=20/1) to afford **9b** (60.0 mg, 83%) as a colorless oil; R_f=0.72 (hexane/ethyl acetate=2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.72 (1H, ddd, J=10.0, 3.7, 3.7 Hz), 5.44 (1H, ddd, J=10.0, 2.2, 2.2 Hz), 3.16 (1H, d, J=7.3 Hz), 2.49–2.39 (2H, m), 2.34–2.28 (1H, m), 2.28–2.19 (2H, m), 2.15–2.08 (2H, m), 1.96 (1H, ddd, J=13.4, 8.3, 2.2 Hz), 1.84–1.62 (4H, m), 1.25 (1H, dd, J=13.7, 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 214.9, 133.3, 127.6, 57.3, 48.3, 47.9, 46.4, 46.0, 40.5, 38.5, 25.5, 24.9, 13.3; IR (neat) ν_{max} 2935, 2856, 1704, 1450, 1228, 1186 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{13}H_{18}OI$: 317.0402, found: 317.0410; $[\alpha]_D^{26}$ +49.6 (c 0.63, $CHCl_3$).

*4.2.36. (1S,9S)-10-Methylidenetricyclo[7.2.1.0^{1,6}]dodec-2-en-7-one (**8**).* To a stirred solution of **9b** (53.2 mg, 0.168 mol) in DMF (1.7 mL) was added DBU (0.0264 mL, 0.177 mmol) and the mixture was stirred at 50 °C for 24 h. The reaction was quenched with saturated aqueous NH_4Cl (1 mL). The aqueous layer was extracted with Et_2O (5 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=50/1) to afford **8** (25.5 mg, 84% (96% conv.)) and recover **9b** (2.3 mg) as a colorless oil; R_f=0.60 (hexane/ethyl acetate=4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.73 (1H, ddd, J=10.2, 3.7, 3.7 Hz), 5.48 (1H, ddd, J=10.2, 2.0, 2.0 Hz), 4.98 (1H, s), 4.94 (1H, s), 2.94–2.87 (1H, m), 2.52 (1H, dd, J=17.3, 3.7 Hz), 2.46–2.22 (4H, m), 2.19–2.09 (2H, m), 1.90–1.65 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 214.9, 152.8, 133.3, 127.5, 108.4, 57.0, 49.9, 47.0, 44.2, 40.8, 40.7, 25.6, 25.1; IR (KBr) ν_{max} 2952, 2883, 1702, 1650, 1330 cm^{-1}; EI HRMS $[M]^+$ calcd for $C_{13}H_{18}O$: 188.1201, found: 188.1203; $[\alpha]_D^{20}$ +93.5 (c 0.55, $CHCl_3$).

*4.2.37. (1S,7S,9S)-10-Methylidenetricyclo[7.2.1.0^{1,6}]dodec-2-en-7-ol (**28**).* To a stirred solution of **8** (1.0 mg, 5.32 10^{-3} mmol) in CH_2Cl_2 (1 mL) was added K-Selectride (1.0 M in THF 0.0226 mL, 2.66×10^{-2} mmol) at −78 °C and the reaction mixture was warmed up to 0 °C and stirred for 1.5 h. The reaction was quenched with saturated aqueous NH_4Cl (1 mL). The aqueous layer was extracted with CH_2Cl_2 (5 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=20/1) to afford alcohol **28** (1.0 mg, quant) as a colorless oil; R_f=0.37 (hexane/ethyl acetate=4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.65 (1H, ddd, J=9.8, 4.9, 2.2 Hz), 5.42 (1H, ddd, J=9.8, 2.0, 2.0 Hz), 5.10 (1H, s), 4.96 (1H, s), 3.68–3.60 (1H, m), 2.72–2.63 (1H, m), 2.48–2.44 (1H, m), 2.29 (1H, ddd, J=16.6, 2.9, 2.9 Hz), 2.22–2.05 (2H, m), 1.97 (1H, ddd, J=14.6, 5.4, 2.7 Hz), 1.94–1.89 (2H, m), 1.69–1.41 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.5, 135.4, 126.9, 106.6, 73.7, 49.0, 46.1, 43.7, 41.3, 41.2, 40.8, 26.4, 25.7; IR (neat) ν_{max} 2925, 1725, 1650, 1434, 1041, 991, 887, 827 cm^{-1}; EI HRMS $[M]^+$ calcd for $C_{13}H_{18}O$: 190.1358, found: 190.1357; $[\alpha]_D^{18}$ −93.5 (c 0.11, $CHCl_3$).

*4.2.38. (1S,3S,4S,5aS,9aS)-1,4,5,8,9,9a-Hexahydro-3-methyl-3H-1,4:3,5a-dimethano-2-benzoxepine (**3**).* To a stirred solution of **28** (3.5 mg, 0.0184 mmol) in CH_2Cl_2 (1 mL) was added TFA (0.2 mL) at 0 °C and the mixture was stirred at the same temperature for 15 min. The reaction was quenched with saturated aqueous $NaHCO_3$ (3 mL) at 0 °C. The aqueous layer was extracted with CH_2Cl_2 (3 mL×2). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate=50/1) to afford **3** (3.0 mg, 86%) as a colorless oil; R_f=0.54 (hexane/ethyl acetate=4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.60 (1H, ddd, J=9.8, 3.7, 3.7 Hz), 5.33 (1H, ddd, J=9.8, 2.0, 2.0 Hz), 4.14 (1H, dd, J=3.4, 3.4 Hz), 2.17–2.07 (3H, m), 1.92–1.73 (4H, m), 1.62–1.42 (5H, m), 1.39 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.2, 126.8, 86.8, 80.6, 52.7, 45.6, 44.9, 44.6, 43.6, 38.3, 26.3, 23.4, 22.3; IR (neat) ν_{max} 2925, 2863, 1727, 1432, 1448, 1377, 1326, 1090, 1039, 997, 823 cm^{-1}; EI HRMS $[M]^+$ calcd for $C_{13}H_{18}O$: 190.1358, found: 190.1352; $[\alpha]_D^{20}$ −35.1 (c 0.09, $CHCl_3$).

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Supplementary data

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