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Facile formation of tetrahydrofurans with multiple chiral centers using double iodoetherification of σ-symmetric diene acetals: short asymmetric total synthesis of rubrenolide and rubrynolide

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Abstract

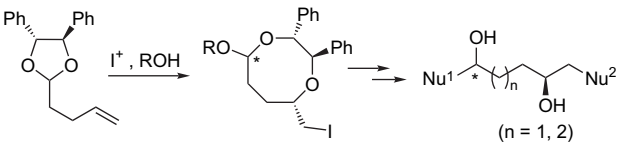
A novel double intramolecular iodoetherification of σ-symmetric diene acetals from (*R*,*R*)-hydrobenzoin occurred in highly diastereoselective manners to give tetrahydrofuran moieties with multiple chiral centers in a one-pot operation. The chemoselective discrimination of the two iodomethyl functions in the products was attained in various reactions. The reaction was applied to the concise asymmetric syntheses of rubrenolide and rubrynolide, in which the unit from the chiral auxiliary worked as a template to achieve the chemoselectivity and as the protecting group of the hydroxyl function.

Keywords: Acyclic diene acetal; Intramolecular haloetherification; Asymmetric synthesis; Rubrenolide; Rubrynolide

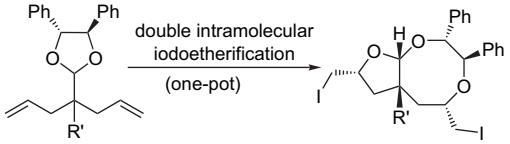
1. Introduction

Tetrahydrofuran or γ-lactone moieties with multiple chiral centers are found in a large number of biologically active natural products.[1] Therefore, the methodology for synthesizing them in a concise manner is highly desirable.

We had recently developed a new asymmetric synthesis of chiral non-racemic 1,4- and 1,5-diol by the intramolecular haloetherification of ene acetals, prepared from ene aldehydes and chiral hydrobenzoin (Eq. 1).[2] As an extension of this reaction, we next studied the reaction of σ-symmetric diene acetals from (*R*,*R*)-hydrobenzoin and found a novel double intramolecular iodoetherification reaction to give tetrahydrofuran moieties with multiple chiral centers. Furthermore, the unit from the chiral auxiliary still remained in the products (Eq. 2).[3] Although several reports on the discrimination of two olefins of an acyclic σ-symmetric diene with a chiral auxiliary by asymmetric intramolecular halolactonization have already been published,[4] there is no domino-type reaction and chiral auxiliaries are removed during the halolactonization by the reported methods.



(1)



(2)

With our reaction, we can form four new asymmetric centers in a single operation and the products still have the unit from the chiral auxiliary. The reaction was then applied to the concise asymmetric synthesis of rubrenolide hoping that the unit from the chiral auxiliary worked as a template

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to achieve the chemoselectivity in further transformations and as the protecting group of the hydroxyl function. We have quite recently communicated these results.[3] We have now studied the reaction in detail, and also succeeded in the asymmetric synthesis of rubrynolide. We now present a full account of our study on the double intramolecular iodoetherification of the acyclic diene acetals and its application to the syntheses of rubrenolide and rubrynolide (Fig. 1).

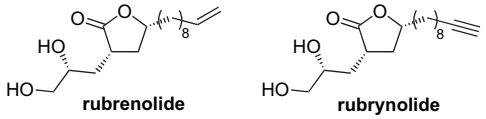


Figure 1. Structure of rubrenolide and rubrynolide.

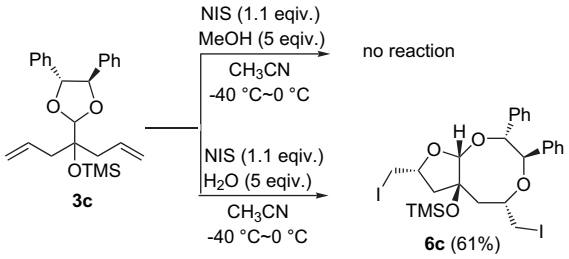
2. Results and discussion

2.1. Preparation of diene acetals

The chiral diene acetals (**2** and **3**) having oxygen functions such as hydroxyl, ether, and ester groups were prepared as follows: (1) the reaction of (*R*,*R*)-hydrobenzoin and dichloroacetic acid with the assist of NaH followed by the formation of methyl ester producing **1**; (2) the reaction of allylmagnesium bromide to **1** leading to the hydroxy diene acetal **2**; and (3) protection of the *tert*-hydroxyl function of **2** by appropriate methods producing compounds **3**. The chiral diene acetals **5a**–**c** having a hydrogen, a phenyl, and a methyl substituent were prepared by acetalization of the diallyl aldehyde **4**[5] with (*R*,*R*)-hydrobenzoin (Scheme 1).

2.2. Intramolecular iodoetherification

We first studied the reactivity of substrate **3c** by treatment with NIS (1.1 equiv) and MeOH (5.0 equiv) in CH_3CN at −40 °C to 0 °C as we already established the conditions in our previous reactions of the ene acetals.[2] However, no reaction occurred and the starting **3c** was recovered. When the reaction was done at rt, the product from the MeOH attack on the olefin in an intermolecular fashion was obtained. We then changed the nucleophile, MeOH, to H_2O. The reaction smoothly proceeded to give **6c** as the major product in a yield of 61%. Other stereoisomers were obtained as a mixture in about 10% yield. Even with the use of 0.5 equiv of NIS, only the two compounds, the recovered **3c** and **6c**, were obtained (Scheme 2).

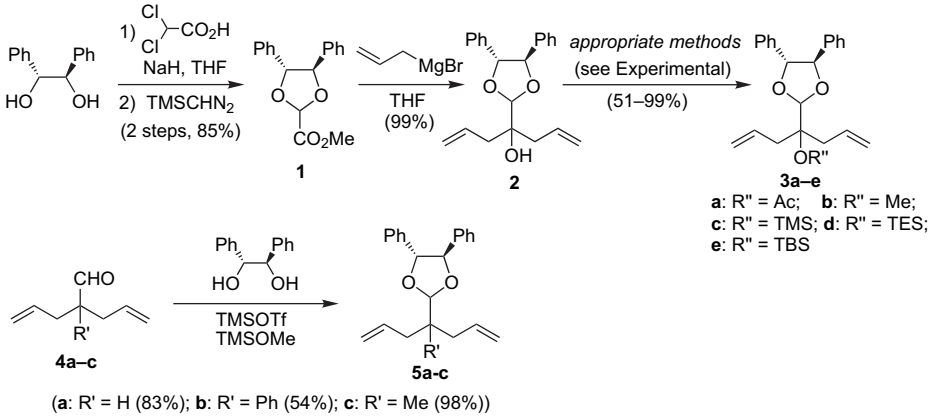


Scheme 2. Reaction of **3c** with NIS in the presence of MeOH or H_2O.

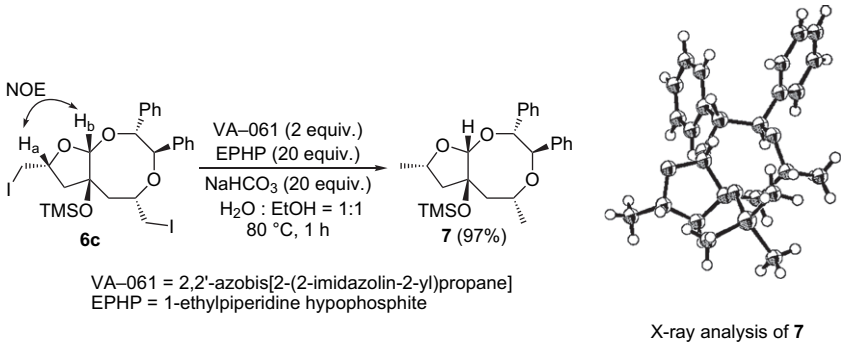
The structure of **6c** was determined as follows. The relationship of the substituents on the five-membered ring was determined by the NOE experiment between two protons, H_a and H_b, and the Me group of the TMS function. The complete structure of the product including the absolute configurations of all of the asymmetric carbon centers was unambiguously determined by X-ray analysis[6] of the dimethyl compound **7** obtained by radical reduction using VA-061[7] of **6c** (Scheme 3).

The optimization of the reaction using H_2O as a nucleophile was studied in detail. These results are shown in Table 1. NBS produced almost the same result as the one by NIS (entry 1). The result in Scheme 2, a 61% yield of **6c**, is shown in entry 2. The use of a greater amount of NIS (2.5 equiv) increased the yield, 64% (entry 3). In entries 1–3, the concentration of the solution is 0.1 M. A greater concentrated reaction mixture (0.5 M) gave a better result, i.e., 73% of **6c** (entry 4). However, the increase in the concentration to 1.0 M resulted in the insolubility of NIS.

This novel reaction proved to be a general reaction. Although the hydroxyl acetal **2** and acetoxy acetal **3a** resulted in decomposition, and the methoxy acetal **3a** resulted in a low yield (entries 1–3), various diene acetals **3c**–**e**, which have an ether group next to the acetal function, and **5a**–**c**, which have a hydrogen, a methyl, and a phenyl group, next to the acetal function, respectively, afforded the double intramolecular iodoetherification products **6c**–**h** as major products in fair to good yields (Table 2). The R_f values between the major stereoisomer and the mixture of other stereoisomers are different



Scheme 1. Preparation of the various acyclic diene acetals.

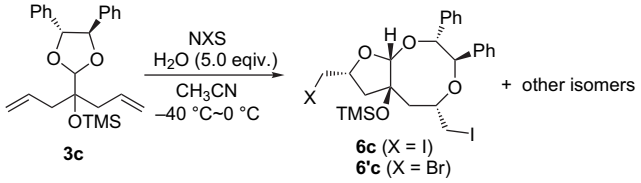


Scheme 3. Radical reduction of **6c** and the X-ray analysis of its reduced product **7**.

from each other (ca. 0.1–0.2 on TLC using hexane/EtOAc as a developing solvent) in every reaction. The isolation of the major isomer as a pure product was easily conducted by usual SiO_2 column chromatography.

Stereochemistry of the major isomer in each reaction was determined as follows. The stereochemistries of **6d**,**e** were determined by comparison of their ^1H and ^{13}C NMR data with those of **6c**, whose stereochemistry was unambiguously determined by the X-ray analysis of its reduction product **7** (see Scheme 4). The stereochemistries of **6f**–**h** were determined by their differential NOE spectra. Thus the presence of NOE between the junctional substituents in each compound showed their cis configuration. The NOEs between the acetal proton and the benzyl proton and between the junctional substituent and the proton next to the iodomethyl group were also observed in each compound. Furthermore, in the case of **6f**, its stereochemistry was unambiguously determined by converting it to rubrenolide and rubrynolide as will be described later (Fig. 2).

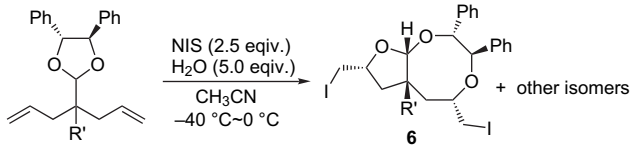
Table 1
Optimization of the double iodoetherification using **3c**



Entry	NXS	equiv	Concentration (M)	Yield[a] (%)
1	NBS	1.1	0.1	60
2	NIS	1.1	0.1	61
3	NIS	2.5	0.1	64
4	NIS	2.5	0.5	73

[a] Yield of the isolated major diastereomer.

Table 2
Intramolecular iodoetherfication of the various diene acetals



Entry	Diene acetal	Time (h)	Total yield (%)	dr[a]	Major product
1	**2** (R′=OH)	—	Decomp.	—	
2	**3a** (R′=OAc)	—	Decomp.	—	
3	**3b** (R′=OMe)	12	38	N.D.[b]	
4	**3c** (R′=OTMS)	1.5	82	8/1	**6c**
5	**3d** (R′=OTES)	3.5	58	11/1	**6d**
6	**3e** (R′=OTBS)	3	84	11/1	**6e**
7	**5a** (R′=H)	3	80	3.5/1	**6f**
8	**5b** (R′=Ph)	3	72	2/1	**6g**
9	**5c** (R′=Me)	13	72	1.5/1	**6h**

[a] Major diastereomer/other diastereomers.
[b] Not determined.

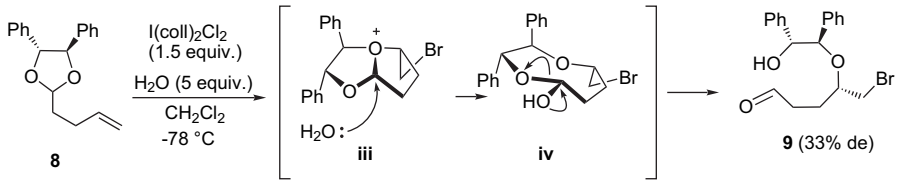
2.3. Reaction mechanism

A mechanistic rationale of the double intramolecular iodoetherification is shown in Scheme 5. The hemiacetal intermediate **ii** was obtained via the oxonium ion intermediate **i**, in which another olefin is present at the proper position. The second intramolecular iodoetherification then occurred to give **6** in good yields. The nucleophilic center of the intermediate **i** is crowded. That is the reason why the larger MeOH than H_2O cannot react (see Scheme 2).

The occurrence of the second intramolecular iodoetherification from the hemiacetal **iv** was unexpected, because the hemiacetal structure of the eight-membered ring usually opens to give the hydroxy aldehyde. Thus the reaction of the ene acetal **8** produced the hydroxyl aldehyde **9** (unpublished result). That is, the NIS treatment of the ene acetal **8** in the presence of H_2O afforded the hydroxyl aldehyde **9** in good yield possibly via the oxonium ion **iii** and then the hemiacetal **iv** (Scheme 4). The only difference between the diene acetals (**2**, **3**, and **5**) and the ene acetal **8** is the presence or absence of one more olefin, which plays an important role.

2.4. Discrimination of two iodomethyl units and the possibility for multi-substituted tetrahydrofurans

Dreiding models and the X-ray structure of **7** showed that compounds **6c**–**h** have the conformations shown in Figure 3, in which the spatial surrounding of the two iodomethyl functions (a) and (b) is completely different. Namely, the iodomethyl group (b) bearing the eight-membered acetal ring is less hindered than the iodomethyl group (a). We then



Scheme 4. Intramolecular iodoetherification of the ene acetal **8** in the presence of H_2O.

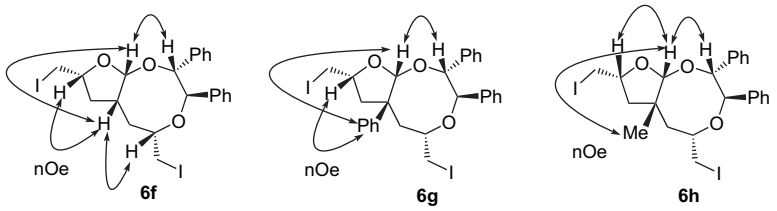
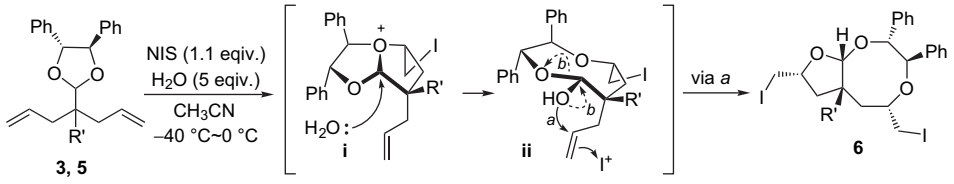


Figure 2. NOE study of compounds **6f–h**.



Scheme 5. Domino-type intramolecular iodoetherification of **3** and **5**.

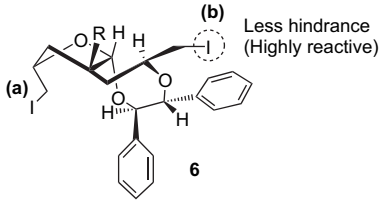


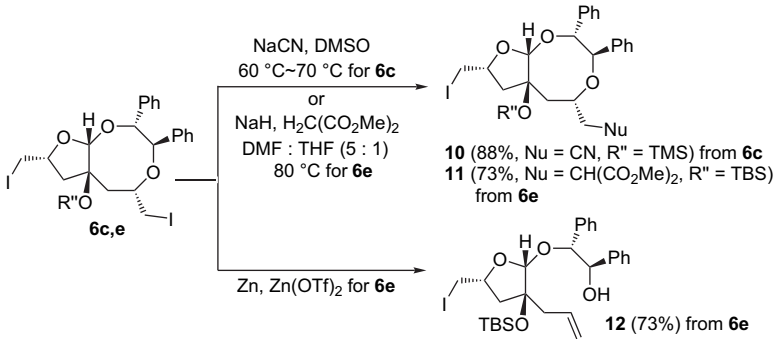
Figure 3. Stereoview of **6**.

considered that the chemoselective reactions on two positions were possible.

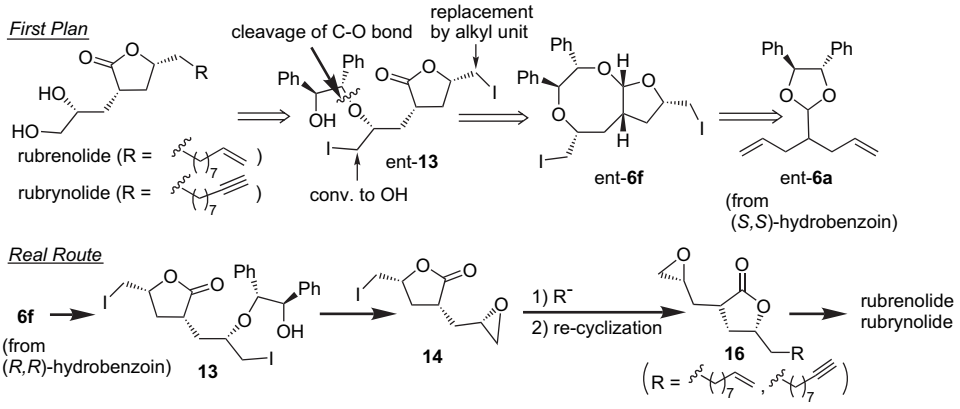
We first examined the nucleophilic substitution reactions using cyano or malonic ester anions. The reaction of **6c** and sodium cyanide[8] gave the product **10**, which was obtained by the selective nucleophilic substitution on the iodomethyl group (b), in good yield. The reaction of **6e** and sodium ethyl malonate[9] also gave the product **11** in the same manner. Furthermore, the deiodoetherification[10] of **6e** selectively occurred on the side of iodine (b) to give **12** in good yield (Scheme 6).

2.5. Application to total syntheses of natural products

As shown above, we succeeded in the remote asymmetric induction of acyclic diene acetals and produced several types of tetrahydrofuran or γ-lactone equivalents with multiple chiral centers in optically active forms. We also proved that the reactivity of the two iodomethyl groups could be controlled to selectively react at one position. We then applied the method to the total syntheses of rubrenolide and rubrynolide.



Scheme 6. Regioselective reactions.



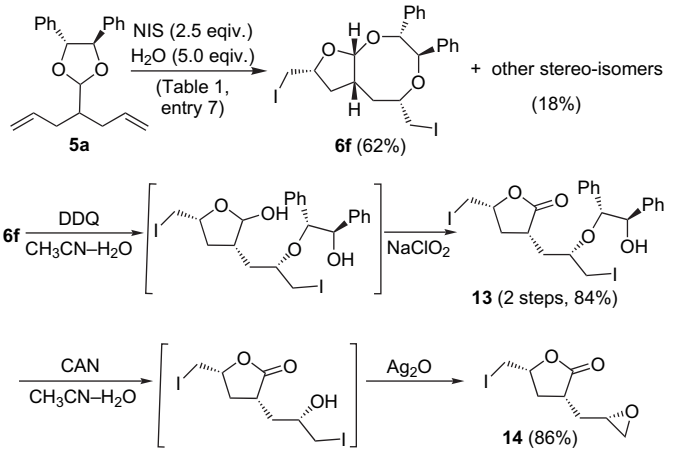
Scheme 7. First plan and real route to the syntheses of rubrenolide and rubrynolide.

Rubrenolide and rubrynolide were isolated from the trunk wood of the Amazonian tree *Nectandra rubra* of the Lauraceae family. They both have a remote asymmetric center in addition to a γ-lactone ring with two asymmetric centers. The only difference between the two compounds is the kind of side chains (alkenyl for rubrenolide and alkynyl for rubrynolide).[11] Asymmetric synthesis of rubrenolide had already been reported.[12] On the other hand, no report on the synthesis of rubrynolide has appeared.

We planned their syntheses from a single intermediate. Our retro-synthetic analysis and abstract of real route are shown in Scheme 7. First, we considered that the lactone *ent*-**13**, which would be derived from *ent*-**6f** obtained by the intramolecular etherification of the diene acetal with (*S*,*S*)-hydrobenzoin, would be the key intermediate, and elongation of the alkenyl or alkynyl unit from the iodo methyl group and conversion of iodine to the hydroxyl group would give two natural products (first plan). However, in fact, we found a novel and easy recyclization of lactone iodide obtained by nucleophilic oxiran ring opening of the epoxy lactone iodide **14** to give the lactone epoxides **16**, which were converted into natural products (real route, vide infra). Compound **6f** from the (*R*,*R*)-hydrobenzoin was then used for the syntheses of the two natural products.

2.5.1. Synthesis of the key intermediate *14*

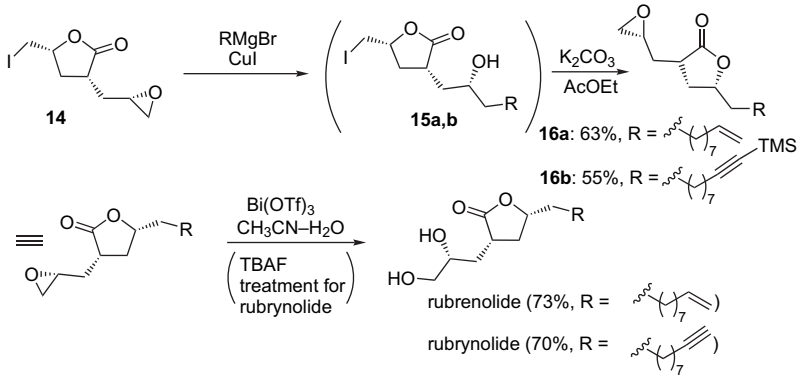
Syntheses of both rubrenolide and rubrynolide were achieved from the same intermediate **14**. The synthesis of the key intermediate **14** is shown in Scheme 8. Although the intramolecular iodoetherification of the diene acetal **5a** produced a 62% yield of **6f** and an 18% yield of the mixture of other stereoisomers, **6f** was easily purified by SiO_2 column chromatography (hexane/AcOEt=20/1). The hydrolysis of **6f** by DDQ treatment[13] afforded the lactol, which was oxidized by $NaClO_2$ to give the lactone **13**. The removal of the hydrobenzoin unit by the usual methods, such as hydrogenation and Birch reduction, afforded unsuccessful results possibly due to the presence of iodines. This conversion was attained by a new method using CAN that was recently developed by us.[14] Thus the treatment of **13** with CAN (2.0 equiv) in CH_3CN/H_2O (1/1) removed the hydrobenzoin unit in high yield. The obtained hydroxyl lactone was rather labile. The hydroxyl lactone was treated with Ag_2O[15] and the more stable epoxy lactone **14** was obtained in good yield (86%).



Scheme 8. Asymmetric synthesis of the key intermediate **14**.

2.5.2. Completion of the syntheses of rubrenolide and rubrynolide

Completion of the syntheses from **14** was achieved as shown in Scheme 9. For the synthesis of rubrenolide, the introduction of the alkenyl side chain was next studied. That is, the reaction of **14** with Grignard reagent[16] from 8-nonenyl bromide in the presence of a catalytic amount of CuI afforded the hydroxyl lactone iodide **15**, which, to our surprise, tended to give the epoxide **16a** by recyclization. The treatment of the hydroxyl lactone with K_2CO_3 then gave the more stable epoxy lactone **16a** in good yield. Opening of the epoxy ring of **16a** with $Bi(OTf)_3$[17] catalyst promoted nucleophilic replacement of water at the primary carbon to give (+)-rubrenolide ($[\alpha]_D^{25}$ +20.5 (*c* 0.29, $CHCl_3$)) in good yield. The authentic rubrenolide was obtained by separation of the mixture of rubrenolide and rubrynolide, which was a generous gift from Prof. B. Zwanenburg and Dr. L. Thijs, according to Ref. 12b. The physical data, $[\alpha]_D$, ^1H NMR, ^{13}C NMR, and IR, of the synthesized (+)-rubrenolide showed good agreement with the authentic one ($[\alpha]_D^{22}$ +22 ($CHCl_3$) in Ref. 11c). Total yield of



Scheme 9. Asymmetric total synthesis of rubrenolide and rubrynolide.

(+)-rubrenolide from the commercially available compound **4a** is 17.1% in nine steps. Since we clarified the reactivity of **14**, **15a**, and **16a** and succeeded in the total synthesis of (+)-rubrenolide, we next tried the synthesis of rubrynolide. In this case, 8-nonynyl bromide was used in place of the 8-nonenyl bromide and the corresponding alkynyl Grignard reagent was prepared.[18] Introduction of the side chain followed by alkaline treatment afforded the epoxy lactone **16b**. The treatment of **16b** with $Bi(OTf)_3$ and TBAF produced the rubrynolide ($[\alpha]_D^{24.5}$ +21.0 (*c* 0.23, $CHCl_3$)). The authentic rubrynolide was obtained by separation of the mixture of rubrenolide and rubrynolide as described above. The physical data, $[\alpha]_D$, ^1H NMR, ^{13}C NMR, and IR, of the synthesized (+)-rubrynolide showed good agreement with the authentic one ($[\alpha]_D^{22}$ +21 ($CHCl_3$) in Ref. 11c). Total yield of (+)-rubrynolide from commercially available compound **4a** is 12.9% in 10 steps.

3. Conclusion

We have developed the unprecedented double intramolecular haloetherifications of the σ-symmetric diene acetals. The reactions proceeded in highly diastereoselective manner to give the tetrahydrofuran units with multiple chiral centers in a one-pot operation. The chemoselective discrimination of the two iodomethyl functions in the products was attained in various reactions. The reaction was applied to the short asymmetric syntheses of (+)-rubrenolide and (+)-rubrynolide. Tetrahydrofuran moieties with multiple chiral centers are found in a large number of biologically active natural products. This method would then provide a useful tool to synthesize them in an enantiomeric form. Further extension of this reaction is currently in progress in our laboratory.

4. Experimental

4.1. General

The ^1H NMR spectra were measured by 300 MHz or 270 MHz spectrometer with tetramethylsilane as the internal standard at 20–25 °C. IR spectra were recorded by a diffuse reflectance measurement of samples dispersed in KBr powder. E. Merck silica gel 60 for column chromatography and E. Merck pre-coated TLC plates, silica gel F_{254}, for preparative thin-layer chromatography were used.

4.2. (4R,5R)-4,5-Diphenyl-2-methoxycarbonyl-1,3-dioxolane (*1*)

A solution of (*R*,*R*)-hydrobenzoin (15.0 g, 0.07 mol) in THF (100 mL) was added dropwise to a suspension of NaH (60% dispersion in mineral oil and washed with Et_2O, 6.16 g, 0.24 mol) in THF (40 mL) at 0 °C under N_2. The mixture was stirred for 30 min at the same temperature. Cl_2CHCO_2H (5.8 mL, 0.07 mol) was added dropwise to the solution at 0 °C and the resulting mixture was refluxed for 3 h. HCl (10%) aqueous solution was added to the solution at 0 °C. The mixture was extracted with AcOEt. Organic layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo. Purification of the residue by SiO_2 column chromatography (AcOEt as an eluent) gave the carboxylic acid (16 g, 0.059 mol, 85%), whose structure was determined by ^1H NMR. ^1H NMR (300 MHz, $CDCl_3$) δ: 4.78 (1H, d, *J*=8.4 Hz), 5.03 (1H, d, *J*=8.4 Hz), 5.81 (1H, s), 7.23–7.32 (10H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 85.6, 86.7, 98.7, 126.6, 126.9, 128.5, 128.5, 134.7, 134.9, 174.1.

$TMSCHN_2$ (2.0 M in hexane, 3.6 mL, 7.20 mmol) was added dropwise to a solution of the above carboxylic acid (1.5 g, 5.60 mmol) in MeOH/benzene (v/v=1/5, 60 mL) and the mixture was stirred for 30 min at rt. The solvent was evaporated in vacuo. Purification of the residue by SiO_2 column chromatography (hexane/AcOEt=5/1 as an eluent) gave **1** (1.54 g, 5.50 mmol, 99%). Colorless crystals: mp 33.0–33.5 °C. $[\alpha]_D^{24.1}$ +51.4 (*c* 1.12, $CHCl_3$). IR (KBr): 1755, 912, 743 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 3.88 (3H, s), 4.76 (1H, d, *J*=8.4 Hz), 5.06 (1H, d, *J*=8.4 Hz), 5.79 (1H, s), 7.21–7.33 (10H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 52.5, 85.5, 86.6, 98.9, 126.6, 127.0, 128.4, 128.5, 135.0, 135.3, 168.9. Anal. Calcd for $C_{17}H_{16}O_4$: C, 71.82; H, 5.67. Found: C, 71.87; H, 5.73.

4.3. (4R,5R)-2-(1-Allyl-1-hydroxy-3-butenyl)-4,5-diphenyl-1,3-dioxolane (*2*)

Allylmagnesium bromide (1.0 M in hexane, 69 mL, 69 mmol) was added dropwise to a solution of **1** (3.90 g, 13.7 mmol) in THF (140 mL) at 0 °C under N_2. The mixture

was stirred for 2 h at the same temperature. Satd NH_4Cl aqueous solution was added to the solution at 0 °C. The mixture was extracted with AcOEt. Organic layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo. Purification of the residue by SiO_2 column chromatography (CH_2Cl_2 as an eluent) gave **2** (4.60 g, 13.6 mmol, 99%). Colorless oil: $[\alpha]_D^{24.1}$ +32.2 (*c* 1.06, $CHCl_3$). IR (KBr): 3562, 912, 743 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.10 (1H, s), 2.49–2.55 (4H, m), 4.78 (2H, s), 5.17–5.23 (4H, m), 5.38 (1H, s), 5.94–6.08 (2H, m), 7.19–7.36 (10H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 39.4, 39.8, 74.4, 85.2, 87.0, 106.7, 118.6, 126.2, 126.7, 128.1, 128.4, 128.5, 128.5, 133.0, 135.9, 137.8. Anal. Calcd for $C_{22}H_{16}O_4$: C, 78.54; H, 7.19. Found: C, 78.44; H, 7.36.

*4.4. (4R,5R)-2-(1-Allyl-1-acetyloxy-3-butenyl)-4,5-diphenyl-1,3-dioxolane (**3a**)*

Ac_2O (0.14 mL, 14.3 mmol) was added dropwise to a solution of **2** (100 mg, 0.30 mmol) and DMAP (3 mg, 0.030 mmol) in pyridine (0.3 mL) at 0 °C under N_2. The mixture was stirred for 12 h at rt. The solvent was evaporated in vacuo. Purification of the residue by SiO_2 column chromatography (hexane/AcOEt=5/1 as an eluent) gave **3a** (57 mg, 0.15 mmol, 51%). Colorless oil: $[\alpha]_D^{26.4}$ +26.3 (*c* 1.09, $CHCl_3$). IR (KBr): 1738, 912, 743 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.06 (3H, s), 2.86–2.99 (4H, m), 4.70 (1H, A in ABq, *J*=8.4 Hz), 4.75 (1H, B in ABq, *J*=8.4 Hz), 5.10–5.21 (4H, m), 5.81 (1H, s), 5.93–6.06 (2H, m), 7.19–7.36 (10H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 22.2, 37.7, 37.8, 84.9, 85.0, 87.0, 105.2, 118.0, 118.2, 126.3, 126.7, 128.1, 128.5, 133.0, 133.0, 135.7, 137.7, 170.0. LRMS (FAB) *m/z* 379 (MH^+). HRMS (FAB) Calcd for $C_{24}H_{27}O_4$: 379.1909. Found: 379.1901.

*4.5. (4R,5R)-2-(1-Allyl-1-methoxy-3-butenyl)-4,5-diphenyl-1,3-dioxolane (**3b**)*

A solution of **2** (100 mg, 0.30 mmol) in THF (0.30 mL) was added dropwise to a suspension of NaH (60% dispersion in mineral oil and washed with Et_2O, 22 mg, 0.55 mmol) in THF (0.3 mL) at 0 °C under N_2. The mixture was stirred for 30 min at the same temperature. MeI (0.034 mL, 0.55 mmol) was added dropwise to the solution at 0 °C and the resulting mixture was stirred for 7 h at rt. Satd NH_4Cl aqueous solution was added to the solution at 0 °C. The mixture was extracted with AcOEt. Organic layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo. Purification of the residue by SiO_2 column chromatography (hexane/AcOEt=20/1 as an eluent) gave **3b** (104 mg, 0.30 mmol, 100%). Colorless oil: $[\alpha]_D^{25.7}$ +18.6 (*c* 1.12, $CHCl_3$). IR (KBr): 1084, 912 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.53–2.70 (4H, m), 3.49 (3H, s), 4.70 (1H, d, *J*=8.4 Hz), 4.72 (1H, d, *J*=8.4 Hz), 5.12–5.23 (4H, m), 5.43 (1H, s), 5.97–6.08 (2H, m), 7.18–7.36 (10H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 36.7, 36.8, 51.5, 78.7, 84.7, 86.9, 107.1, 117.7, 126.2, 126.8, 128.0, 128.4, 133.6, 136.1, 138.3. Anal. Calcd for $C_{23}H_{26}O_3$: C, 78.83; H, 7.48. Found: C, 78.75; H, 7.59.

*4.6. (4R,5R)-2-(1-Allyl-1-trimethylsilyloxy-3-butenyl)-4,5-diphenyl-1,3-dioxolane (**3c**)*

Et_3N (0.22 mL, 1.60 mmol) and TMSCl (0.10 mL, 0.80 mmol) were added dropwise to a solution of **2** (147 mg, 0.40 mmol) and DMAP (4 mg, 0.040 mmol) in CH_2Cl_2 (0.8 mL) at 0 °C under N_2. The mixture was stirred for 12 h at rt. Satd $NaHCO_3$ aqueous solution was added to the solution at 0 °C. The mixture was extracted with AcOEt. Organic layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo. Purification of the residue by SiO_2 column chromatography (hexane/AcOEt=10/1 as an eluent) gave **3c** (162 mg, 0.40 mmol, 99%). Colorless oil: $[\alpha]_D^{25.9}$ +16.2 (*c* 1.04, $CHCl_3$). IR (KBr): 1248, 912, 743 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.15 (9H, s), 2.47–2.56 (4H, m), 4.67 (2H, s), 5.07–5.17 (4H, m), 5.32 (1H, s), 5.88–6.07 (2H, m), 7.16–7.31 (10H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 2.8 (3C), 40.3, 40.3, 78.5, 85.2, 86.9, 107.0, 117.5, 117.6, 126.3, 126.7, 128.0, 128.4, 134.1, 136.2, 138.1. Anal. Calcd for $C_{25}H_{32}O_3Si$: C, 73.49; H, 7.89. Found: C, 73.66; H, 7.97.

*4.7. (4R,5R)-2-(1-Allyl-1-triethylsilyloxy-3-butenyl)-4,5-diphenyl-1,3-dioxolane (**3d**)*

TESOTf (1.68 mL, 7.40 mmol) was added dropwise to a solution of **2** (500 mg, 1.50 mmol) and 2,6-lutidine (1.73 mL, 14.9 mmol) in CH_2Cl_2 (1.5 mL) at 0 °C under N_2. The mixture was allowed to gradually warm to rt. Satd $NaHCO_3$ aqueous solution was added to the solution at 0 °C. The mixture was extracted with AcOEt. Organic layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo. Purification of the residue by SiO_2 column chromatography (hexane/AcOEt=50/1 as an eluent) gave **3d** (636 mg, 1.40 mmol, 93%). Colorless oil: $[\alpha]_D^{25.6}$ +4.9 (*c* 1.12, $CHCl_3$). IR (KBr): 1240, 912 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.59 (6H, q, *J*=8.4 Hz), 0.88 (9H, t, *J*=8.4 Hz), 2.43–2.45 (4H, m), 4.57 (1H, d, *J*=8.4 Hz), 4.61 (1H, d, *J*=8.4 Hz), 5.01–5.11 (4H, m), 5.27 (1H, s), 5.92–5.94 (2H, m), 7.10–7.27 (10H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 7.0 (3C), 7.3 (3C), 40.7, 40.7, 78.0, 85.0, 86.9, 107.2, 117.4, 117.5, 126.3, 126.7, 127.9, 128.3, 134.3, 136.2, 138.2. Anal. Calcd for $C_{28}H_{38}O_3Si$: C, 74.62; H, 8.50. Found: C, 74.45; H, 8.56.

*4.8. (4R,5R)-2-[1-Allyl-1-tert-butyldimethylsilyloxy-3-butenyl]-4,5-diphenyl-1,3-dioxolane (**3e**)*

TBSOTf (1.71 mL, 7.40 mmol) was added dropwise to a solution of **2** (500 mg, 1.50 mmol) and 2,6-lutidine (1.73 mL, 14.9 mmol) in CH_2Cl_2 (1.5 mL) at 0 °C under N_2. The mixture was allowed to gradually warm to rt and stirred for 12 h at the same temperature. Satd $NaHCO_3$ aqueous solution was added to the solution at 0 °C. The mixture was extracted with AcOEt. Organic layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo. Purification of the residue by SiO_2 column chromatography (hexane/AcOEt=50/1 as an eluent) gave **3e** (615 mg, 1.40 mmol, 90%). Colorless oil: $[\alpha]_D^{25.7}$ −13.8

(*c* 0.50, $CHCl_3$). IR (KBr): 1252, 912 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.01 (3H, s), 0.06 (3H, s), 0.79 (9H, s), 2.41–2.45 (4H, m), 4.54 (1H, d, *J*=8.3 Hz), 4.57 (2H, d, *J*=8.3 Hz), 4.97–5.08 (4H, m), 5.23 (1H, s), 5.87–5.97 (2H, m), 7.07–7.24 (10H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: −2.0 (2C), 18.9, 26.2 (3C), 40.4, 40.7, 78.2, 85.0, 86.9, 107.1, 117.4, 117.6, 126.3, 126.6, 128.0, 128.4, 134.2, 136.0, 138.0. Anal. Calcd for $C_{28}H_{38}O_3Si$: C, 74.62; H, 8.50. Found: C, 74.60; H, 8.60.

*4.9. (4R,5R)-2-(1-Allyl-3-butenyl)-4,5-diphenyl-1,3-dioxolane (**5a**)*

A solution of (*R*,*R*)-hydrobenzoin (340 mg, 1.60 mmol) in THF (1.0 mL) and TMSOMe (0.89 mL, 6.40 mmol) was added dropwise to a solution of the known and commercially available **4a** (100 mg, 0.81 mmol) in THF (0.6 mL) at −78 °C under N_2. TMSOTf (0.015 mL, 0.081 mmol) was added to the mixture and the resulting solution was allowed to gradually warm to rt and stirred for 24 h. Satd NH_4Cl aqueous solution was added to the solution. The mixture was extracted with AcOEt. Organic layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo. Purification of the residue by SiO_2 column chromatography (hexane/AcOEt=30/1 as an eluent) gave **5a** (214 mg, 0.66 mmol, 83%). Colorless oil: $[\alpha]_D^{23.5}$ −30.9 (*c* 1.19, $CHCl_3$). IR (KBr): 912, 748 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.00 (1H, m), 2.21–2.28 (2H, m), 2.36–2.38 (2H, m), 4.62 (1H, d, *J*=8.4 Hz), 4.66 (1H, d, *J*=8.4 Hz), 4.99–5.09 (4H, m), 5.42 (1H, d, *J*=3.3 Hz), 5.80–5.89 (2H, m), 7.12–7.28 (10H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 33.0, 33.1, 41.8, 85.0, 86.8, 106.4, 116.4, 126.2, 126.7, 127.9, 128.4, 136.5, 136.6, 138.5. Anal. Calcd for $C_{22}H_{24}O_2$: C, 82.46; H, 7.55. Found: C, 82.40; H, 7.69.

*4.10. (4R,5R)-2-(1-Allyl-1-phenyl-3-butenyl)-4,5-diphenyl-1,3-dioxolane (**5b**)*

A solution of (*R*,*R*)-hydrobenzoin (2.8 g, 13.0 mmol) in THF (5.0 mL) and TMSOMe (7.2 mL, 52.0 mmol) was added dropwise to a solution of the known **4b** (1.3 g, 6.50 mmol) in THF (8.0 mL) at −78 °C under N_2. TMSOTf (0.12 mL, 0.65 mmol) was added to the mixture and the resulting solution was allowed to gradually warm to rt and stirred for 24 h. Satd NH_4Cl aqueous solution was added to the solution. The mixture was extracted with AcOEt. Organic layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo. Purification of the residue by SiO_2 column chromatography (hexane/AcOEt=50/1 as an eluent) gave **5b** (1.4 g, 3.50 mmol, 54%). Colorless oil: $[\alpha]_D^{26.1}$ +25.7 (*c* 1.09, $CHCl_3$). IR (KBr): 912, 743 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.94 (4H, t, *J*=7.5 Hz), 4.26 (1H, d, *J*=8.4 Hz), 4.66 (1H, d, *J*=8.4 Hz), 5.14–5.35 (4H, m), 5.65 (1H, s), 5.82–6.01 (2H, m), 7.00–7.94 (15H, m); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 37.3, 37.9, 47.8, 84.8, 86.8, 108.1, 117.8, 117.9, 126.2, 126.3, 127.0, 127.6, 127.9, 128.2, 128.3, 128.8, 134.2, 136.0, 138.2, 140.9. LRMS (FAB) *m/z* 419 (MNa^+). HRMS (FAB) Calcd for $C_{28}H_{28}NaO_2$: 419.1987. Found: 419.1983.

*4.11. (4R,5R)-2-(1-Allyl-1-methyl-3-butenyl)-4,5-diphenyl-1,3-dioxolane (**5c**)*

A solution of (*R*,*R*)-hydrobenzoin (1.0 g, 4.80 mmol) in THF (2.0 mL) and TMSOMe (2.7 mL, 11.3 mmol) was added dropwise to a solution of the known **4c** (367 mg, 2.40 mmol) in THF (3.0 mL) at −78 °C under N_2. TMSOTf (0.05 mL, 0.28 mmol) was added to the mixture and the resulting solution was allowed to gradually warm to rt and stirred for 24 h. Satd NH_4Cl aqueous solution was added to the solution. The mixture was extracted with AcOEt. Organic layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo. Purification of the residue by SiO_2 column chromatography (hexane/AcOEt=50/1 as an eluent) gave **5c** (820 mg, 2.35 mmol, 98%). Colorless oil: $[\alpha]_D^{25.0}$ +24.9 (*c* 1.34, $CHCl_3$). IR (KBr): 912, 749 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.09 (3H, s), 2.30–2.33 (4H, m), 4.64 (1H, d, *J*=8.4 Hz), 4.70 (1H, d, *J*=8.4 Hz), 5.10–5.16 (4H, m), 5.26 (1H, s), 5.89–6.01 (2H, m), 7.18–7.36 (10H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 19.3, 39.5, 39.7, 40.7, 85.2, 86.9, 109.3, 117.6, 126.3, 126.8, 128.0, 128.5, 134.7, 136.6, 138.8. Anal. Calcd for $C_{23}H_{26}O_2$: C, 82.60; H, 7.84. Found: C, 82.68; H, 7.83.

4.12. General procedure for an intramolecular haloetherification

NIS (5 mmol) was added to a solution of the diene acetal (1 mmol) in CH_3CN (2 mL) at −40 °C under N_2 and the mixture was stirred for 30 min at the same temperature. H_2O (5 mmol) was added to the resulting mixture, which was allowed to warm to 0 °C for over 40 min. Satd $Na_2S_2O_3$ aqueous solution was added to the mixture, which was extracted with Et_2O. The organic layer was washed with brine, dried over $MgSO_4$, and evaporated in vacuo. The residue was purified by SiO_2 column chromatography using hexane/AcOEt to give the product and other diastereomixture.

*4.12.1. (1S,3R,4R,6S,8S,10R)-6,10-Bis(iodomethyl)-3,4-diphenyl-8-trimethylsilyloxy-2,5,11-trioxabicyclo[6.3.0]-undecane (**6c**)*

Compound **6c** (62 mg, 0.092 mmol) and other diastereomeric mixture (8 mg, 0.011 mmol) were obtained in total 82% from **3c** (51 mg, 0.13 mmol), NIS (141 mg, 0.63 mmol), and H_2O (0.011 mL, 0.63 mmol). Hexane/AcOEt=20/1. Amorphous: $[\alpha]_D^{24.8}$ +50.4 (*c* 1.04, $CHCl_3$). IR (KBr): 1016, 912, 741 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.82 (1H, dd, *J*=13.5, 4.5 Hz), 2.38–2.94 (2H, m), 2.48 (1H, dd, *J*=13.5, 6.0 Hz), 3.03 (1H, dd, *J*=9.3, 9.2 Hz), 3.12 (1H, d, *J*=7.5 Hz), 3.34 (1H, dd, *J*=9.3, 4.8 Hz), 4.38–4.41 (4H, m), 4.39 (1H, d, *J*=8.4 Hz), 4.54 (1H, d, *J*=8.4 Hz), 5.69 (1H, s), 6.81–6.89 (4H, m), 7.07–7.13 (6H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 2.3 (3C), 5.7, 10.8, 37.8, 44.2, 74.6, 78.1, 79.8, 85.1, 87.0, 111.3, 127.2, 127.3, 127.5, 127.6, 127.7, 127.8, 138.2, 139.0. LRMS (FAB) *m/z* 679 (MH^+). HRMS (FAB) Calcd for $C_{25}H_{33}I_2O_4Si$: 679.0267. Found: 679.0267.

4.12.2. (1S,3R,4R,6S,10R)-6,10-Bis(iodomethyl)-3,4-diphenyl-8-methoxy-2,5,11-trioxabicyclo[6.3.0]-undecane (**6b**)

Compound **6b** (18 mg, 0.029 mmol, diastereomeric mixture, total 38%) was obtained from **3b** (27 mg, 0.077 mmol), NIS (87 mg, 0.39 mmol), and H_2O (0.007 mL, 0.39 mmol). Colorless crystals: mp 175.5–176.0 °C. $[\alpha]_D^{25.7}$ +44.2 (*c* 1.07, $CHCl_3$). IR (KBr): 1096, 912, 740 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.60 (1H, dd, *J*=13.8, 9.3 Hz), 2.17 (1H, dd, *J*=15.6, 12.0 Hz), 2.63–2.74 (2H, m), 3.05–3.15 (3H, m), 3.15–3.38 (1H, m), 3.35 (3H, s), 4.30–4.43 (2H, m), 4.42 (1H, d, *J*=8.4 Hz), 4.57 (1H, d, *J*=8.4 Hz), 5.73 (1H, s), 6.84–6.89 (4H, m), 7.09–7.26 (6H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 5.8, 10.7, 31.9, 37.7, 50.0, 74.4, 77.8, 79.9, 87.3, 110.4, 127.1, 127.5, 127.5, 127.6, 127.7, 137.9, 138.7. LRMS (FAB) *m/z* 621 (MH^+). HRMS (FAB) Calcd for $C_{23}H_{27}I_2O_4$: 620.9999. Found: 620.9974.

4.12.3. (1S,3R,4R,6S,8S,10R)-6,10-Bis(iodomethyl)-3,4-diphenyl-8-triethylsilyloxy-2,5,11-trioxabicyclo[6.3.0]-undecane (**6d**)

Compound **6d** (67 mg, 0.15 mmol) and other diastereomeric mixture (5 mg, 0.007 mmol) were obtained in total 58% from **3d** (67 mg, 0.15 mmol), NIS (166 mg, 0.74 mmol), and H_2O (0.013 mL, 0.74 mmol). Hexane/AcOEt=20/1. Amorphous: $[\alpha]_D^{24.5}$ +35.2 (*c* 1.12, $CHCl_3$). IR (KBr): 1170, 912, 743 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.65 (6H, q, *J*=7.8 Hz), 0.96 (9H, t, *J*=7.8 Hz), 1.78 (1H, dd, *J*=13.8, 5.1 Hz), 2.24–2.43 (3H, m), 2.96 (1H, t, *J*=9.3 Hz), 3.05 (2H, d, *J*=6.9 Hz), 3.27 (1H, dd, *J*=9.3, 4.8 Hz), 4.32–4.46 (2H, m), 4.34 (1H, d, *J*=8.4 Hz), 4.47 (1H, d, *J*=8.4 Hz), 5.60 (1H, s), 6.75–6.82 (4H, m), 7.02–7.18 (6H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 7.3 (3C), 8.0 (3C), 12.1, 39.2, 45.5, 75.2, 78.9, 80.4, 85.6, 87.7, 112.0, 127.8, 127.9, 128.1, 128.2, 128.4, 138.9, 139.6. Anal. Calcd for $C_{28}H_{38}I_2O_4Si$: C, 46.68; H, 5.32; I, 35.23. Found: C, 46.69; H, 5.21; I, 35.18.

4.12.4. (1S,3R,4R,6S,8S,10R)-6,10-Bis(iodomethyl)-3,4-diphenyl-8-tert-butyldimethylsilyloxy-2,5,11-trioxabicyclo-[6.3.0]undecane (**6e**)

Compound **6e** (67 mg, 0.093 mmol) and other diastereomeric mixture (6 mg, 0.009 mmol) were obtained in total 84% from **3e** (55 mg, 0.12 mmol), NIS (137 mg, 0.61 mmol), and H_2O (0.011 mL, 0.61 mmol). Hexane/AcOEt=20/1. Amorphous: $[\alpha]_D^{24.3}$ +40.9 (*c* 1.01, $CHCl_3$). IR (KBr): 1015, 912, 740 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.23 (6H, s), 0.93 (9H, s), 1.84 (1H, dd, *J*=13.5, 4.8 Hz), 2.30 (1H, dd, *J*=12.0, 2.0 Hz), 2.41–2.51 (2H, m), 3.02 (1H, t, *J*=9.3 Hz), 3.10 (2H, d, *J*=7.2 Hz), 3.32 (1H, dd, *J*=9.3, 4.5 Hz), 4.39 (1H, d, *J*=8.4 Hz), 4.55 (1H, d, *J*=8.4 Hz), 4.38–4.55 (2H, m), 5.68 (1H, s), 6.81–6.88 (4H, m), 7.08–7.12 (6H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: −1.6, −1.6, 6.5, 12.0, 19.2, 26.7 (3C), 38.9, 45.3, 75.1, 77.9, 80.4, 85.8, 87.7, 111.8, 127.8, 127.9, 128.1, 128.2, 128.3, 128.4, 138.9, 139.6. Anal. Calcd for $C_{28}H_{38}I_2O_4Si$: C, 46.68; H, 5.32; I, 35.23. Found: C, 46.46; H, 5.34; I, 34.98.

4.12.5. (1S,3R,4R,6S,8R,10R)-6,10-Bis(iodomethyl)-3,4-diphenyl-2,5,11-trioxabicyclo[6.3.0]undecane (**6f**)

Compound **6f** (114 mg, 0.19 mmol, 62%) and other diastereomeric mixture (33 mg, 0.056 mmol, 18%) were obtained from **5a** (100 mg, 0.31 mmol), NIS (351 mg, 1.60 mmol), and H_2O (0.028 mL, 1.60 mmol). Hexane/AcOEt=20/1. Amorphous: $[\alpha]_D^{23.9}$ +65.4 (*c* 1.12, $CHCl_3$). IR (KBr): 1042, 912, 743 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.98–2.03 (2H, m), 2.10–2.23 (1H, m), 2.40–2.42 (2H, m), 3.00–3.07 (3H, m), 3.28 (1H, dd, *J*=9.3, 4.5 Hz), 4.03–4.25 (2H, m), 4.32 (1H, d, *J*=8.4 Hz), 4.44 (1H, d, *J*=8.4 Hz), 5.89 (1H, d, *J*=4.5 Hz), 6.79–6.72 (4H, m), 7.04–7.19 (6H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 6.3, 32.5, 35.4, 38.2, 65.3, 76.7, 77.4, 87.8, 127.0, 127.1, 127.8, 127.9, 128.0, 128.1, 128.3, 128.4, 128.5, 128.6, 128.7, 138.7, 139.4, 178.0. LRMS (FAB) *m/z* 591 (MH^+). HRMS (FAB) Calcd for $C_{22}H_{25}I_2O_3$: 590.9893. Found: 590.9875.

4.12.6. (1S,3R,4R,6S,8R,10R)-6,10-Bis(iodomethyl)-3,4,8-triphenyl-2,5,11-trioxabicyclo[6.3.0]undecane (**6g**)

Compound **6g** (167 mg, 0.25 mmol) and its diastereomeric mixture (83 mg, 0.13 mmol) in total 72% were obtained from **5b** (207 mg, 0.52 mmol), NIS (587 mg, 2.61 mmol), and H_2O (0.047 mL, 2.61 mmol). Colorless amorphous: $[\alpha]_D^{25.9}$ +58.5 (*c* 1.00, $CHCl_3$). IR (KBr): 1076, 912, 739 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.48–2.60 (4H, m), 2.96–3.05 (3H, m), 3.23 (1H, dd, *J*=9.6, 5.1 Hz), 3.68–3.90 (2H, m), 4.39 (1H, d, *J*=8.4 Hz), 4.61 (1H, d, *J*=8.4 Hz), 6.3 (1H, s), 6.80–7.47 (15H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 5.9, 10.5, 38.7, 45.8, 55.6, 75.8, 80.0, 87.4, 109.1, 126.5, 126.9, 127.2, 127.3, 127.5, 127.6, 127.7, 128.8, 138.3, 138.8, 141.1. LRMS (FAB) *m/z* 667 (MH^+). HRMS (FAB) Calcd for $C_{28}H_{29}I_2O_3$: 667.0206. Found: 667.0211.

4.12.7. (1S,3R,4R,6S,8R,10R)-6,10-Bis(iodomethyl)-3,4-diphenyl-8-methyl-2,5,11-trioxabicyclo[6.3.0]undecane (**6h**)

Compound **6h** (74 mg, 0.12 mmol) and its diastereomeric mixture (48 mg, 0.079 mmol) in total 72% yield were obtained from **5c** (94 mg, 0.28 mmol), NIS (316 mg, 1.41 mmol), and H_2O (0.025 mL, 1.41 mmol). Colorless amorphous: $[\alpha]_D^{24.3}$ −17.2 (*c* 1.15, $CHCl_3$). IR (KBr): 1041, 912, 743 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.34 (3H, s), 1.68 (1H, dd, *J*=10.9, 5.4 Hz), 1.83 (1H, dd, *J*=14.9, 10.6 Hz), 2.04–2.17 (2H, m), 2.76–2.77 (2H, m), 3.17 (1H, dd, *J*=9.7, 7.8 Hz), 3.27 (1H, dd, *J*=4.6, 2.3 Hz), 4.15–4.22 (2H, m), 4.69 (1H, d, *J*=9.3 Hz), 4.91 (1H, d, *J*=9.34 Hz), 5.80 (1H, s), 7.01–7.09 (10H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 9.4, 12.0, 22.8, 40.3, 44.5, 45.9, 73.0, 74.0, 81.4, 84.1, 109.2, 127.4, 127.6, 127.7, 127.9, 128.0, 128.2. LRMS (FAB) *m/z* 605 (MH^+). HRMS (FAB) Calcd for $C_{23}H_{27}I_2O_3$: 605.0050. Found: 605.0048.

4.13. (1R,3R,4R,6R,8S,10S)-6,10-Bismethyl-3,4-diphenyl-8-trimethylsilyloxy-2,5,11-trioxabicyclo[6.3.0]undecane (**7**) (reaction in Scheme 3)

$NaHCO_3$ (74 mg, 0.88 mmol), EPHP (158 mg, 0.88 mmol), and VA-061 (29 mg, 0.088 mmol) were added successively to

a solution of **6c** (30 mg, 0.044 mmol) in EtOH/H_2O (v/v=1/1, 1.0 mL) at rt under N_2, and the mixture was stirred for 1 h at 80 °C. The reaction mixture was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by SiO_2 column chromatography (benzene as an eluent) to give **7** (18 mg, 0.043 mmol, 97%). Colorless crystals: mp 95.0–95.5 °C. $[\alpha]_D^{25.6}$ +38.5 (*c* 1.10, $CHCl_3$). IR (KBr): 1146, 912 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.01 (9H, s), 0.89 (3H, d, *J*=6.8 Hz), 1.09 (3H, d, *J*=6.2 Hz), 1.50–1.60 (2H, m), 1.96 (1H, dd, *J*=13.1, 5.6 Hz), 2.16 (1H, dd, *J*=14.9, 12.3 Hz), 4.19 (1H, d, *J*=8.8 Hz), 4.08–4.27 (2H, m), 4.35 (1H, d, *J*=8.8 Hz), 5.36 (1H, s), 6.64–6.74 (4H, m), 6.86–6.90 (6H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 2.4 (3C), 19.0, 23.0, 41.3, 45.2, 69.1, 73.8, 78.9, 85.6, 86.8, 110.8, 127.0, 127.2, 127.3, 127.6, 138.9, 140.1. Anal. Calcd for $C_{25}H_{34}O_4Si$: C, 70.38; H, 8.03. Found: C, 70.48; H, 8.05.

*4.14. (1S,3R,4R,6R,8S,10R)-6-Cyanomethyl-10-iodomethyl-3,4-diphenyl-8-trimethylsilyloxy-2,5,11-trioxabicyclo-[6.3.0]undecane (**10**) (reaction in Scheme 6)*

NaCN (4 mg, 0.088 mmol) was added to a solution of **6c** (40 mg, 0.059 mmol) in DMSO (1.2 mL) at rt under N_2 and the mixture was stirred for 2 h at 60–70 °C. After completion of the reaction (TLC check), satd $Na_2S_2O_3$ aqueous solution was added to the mixture, which was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by SiO_2 column chromatography (hexane/AcOEt=5/1 as an eluent) to give **10** (30 mg, 0.052 mmol, 88%). Colorless crystals: mp 112.0–112.5 °C. $[\alpha]_D^{25.2}$ +70.3 (*c* 1.07, $CHCl_3$). IR (KBr): 2358, 1252, 912, 743 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.24 (9H, s), 1.84 (1H, dd, *J*=13.5, 4.5 Hz), 2.08 (1H, dd, *J*=14.7, 2.1 Hz), 2.45–2.53 (4H, m), 3.04 (1H, t, *J*=9.3 Hz), 3.34 (1H, dd, *J*=9.6, 4.8 Hz), 4.38–4.47 (1H, m), 4.53–4.60 (1H, m), 4.46 (1H, d, *J*=8.4 Hz), 4.54 (1H, d, *J*=8.4 Hz), 5.65 (1H, s), 6.81–6.88 (4H, m), 7.08–7.13 (6H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 2.2, 10.6, 22.2, 38.6, 44.1, 69.3, 78.1, 80.2, 84.9, 87.0, 111.4, 117.0, 127.2, 127.3, 127.6, 127.7, 127.8, 128.0, 137.9, 138.1. Anal. Calcd for $C_{26}H_{32}INO_4Si$: C, 54.07; H, 5.58; N, 2.43; I, 21.97. Found: C, 54.22; H, 5.63; N, 2.36; I, 21.88.

*4.15. (1S,3R,4R,6R,8S,10R)-6-[2,2-Bis(methoxycarboyl)-ethyl]-10-iodomethyl-3,4-diphenyl-8-tert-butyldimethyl-silyloxy-2,5,11-trioxabicyclo[6.3.0]undecane (**11**) (reaction in Scheme 6)*

Dimethyl malonate (0.025 mL, 0.21 mmol) was added dropwise to a solution of NaH (9 mg, 0.211 mmol, 60% dispersion in mineral oil, washed with dry Et_2O) in DMF (0.5 mL) at 0 °C under N_2. The mixture was stirred for 30 min at the same temperature. A solution of **6e** (32 mg, 0.044 mmol) in THF (0.1 mL) was added to a resulting solution at 0 °C and the mixture was stirred for 4 h at 80 °C. Satd NH_4Cl aqueous solution was added to the mixture, which was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by SiO_2 column chromatography (hexane/AcOEt=5/1 as an eluent) to give **11** (23 mg, 0.032 mmol, 73%). Colorless oil: $[\alpha]_D^{25.2}$ +96.0 (*c* 1.01, $CHCl_3$). IR (KBr): 1736, 1436, 1037, 773 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.03 (3H, s), 0.06 (3H, s), 0.71 (9H, s), 1.60–1.73 (2H, m), 1.83–1.93 (2H, m), 2.13–2.26 (2H, m), 2.79–2.87 (2H, m), 3.10–3.15 (1H, m), 3.20 (3H, s), 3.46 (3H, s), 4.00–4.08 (1H, m), 4.12–4.23 (1H, m), 4.13 (1H, d, *J*=8.4 Hz), 4.34 (1H, d, *J*=8.4 Hz), 5.49 (1H, s), 6.62–6.69 (4H, m), 6.87–6.89 (6H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: −2.7, −2.4, 11.2, 18.5, 25.9 (3C), 31.6, 40.0, 44.6, 47.7, 52.3, 52.5, 70.9, 77.0, 77.5, 79.0, 85.0, 87.0, 111.2, 127.1, 127.5, 138.3, 138.7, 169.3, 139.5. Anal. Calcd for $C_{32}H_{43}IO_8Si$: C, 54.69; H, 6.26; I, 17.51. Found: C, 54.70; H, 6.17; I, 17.59.

*4.16. (1R,2R)-2-[(2S,3S,5R)-3-Allyl-3-tert-butyldimethyl-silyloxy-5-iodomethyl-2-tetrahydrofuranyloxy]-1,2-diphenylethanol (**12**) (reaction in Scheme 6)*

$Zn(OTf)_2$ (20 mg, 0.055 mmol) was added to a solution of **6e** (31 mg, 0.043 mmol) in THF (0.5 mL) under N_2. The mixture was stirred for 30 min at 50 °C. Zn (34 mg, 0.34 mmol) was added to the resulting solution, which was additionally stirred for 5 h at 70 °C. Et_2O was added to the mixture. Precipitated salt was filtered. The filtrate was washed with brine, dried over $MgSO_4$, and evaporated in vacuo. The residue was purified by SiO_2 column chromatography (hexane/AcOEt=20/1 as an eluent) to give **12** (19 mg, 0.031 mmol, 73%). Colorless oil: $[\alpha]_D^{26.6}$ +104.4 (*c* 1.09, $CHCl_3$). IR (KBr): 1068, 1011, 698 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.09 (6H, s), 0.85 (9H, s), 1.57 (1H, dd, *J*=13.0, 9.6 Hz), 2.18–2.24 (2H, m), 2.42–2.45 (1H, m), 2.63 (2H, d, *J*=6.4 Hz), 4.22–4.33 (1H, m), 4.52 (1H, d, *J*=7.9 Hz), 4.69 (1H, d, *J*=7.9 Hz), 5.10 (1H, s), 5.23–5.28 (2H, m), 6.07–6.13 (1H, m), 7.01–7.04 (4H, m), 7.13–7.17 (6H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: −2.4, −2.3, 8.7, 18.4, 25.8 (3C), 40.4, 43.7, 77.0, 78.6, 79.7, 85.0, 85.8, 109.8, 117.6, 127.0, 127.5, 127.6, 127.8, 134.9, 139.5. LRMS (FAB) *m/z* 379 (MH^+). HRMS (FAB) Calcd for $C_{28}H_{40}IO_4Si$: 617.1560. Found: 617.1556.

*4.17. (3R,5R)-3-{2-(S)-[(1R,2R)-2-Hydroxy-1,2-diphenylethoxy]-3-iodopropyl}-5-iodomethyl-dihydrofuran-2-one (**13**)*

DDQ (58 mg, 0.25 mmol) was added to a solution of **6f** (100 mg, 0.17 mmol) in CH_3CN/H_2O (v/v=10/1, 1.8 mL). The mixture was stirred for 2 h at 60 °C. Satd $NaHCO_3$ aqueous solution was added to the mixture, which was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by SiO_2 column chromatography (hexane/AcOEt=2/1 as an eluent) to give **6f** (36 mg, 0.061 mmol) and the hemiacetal (60 mg, 0.099 mmol, 58% (91% based on the consumed **6f**)). Amorphous: IR (KBr): 3400, 1020, 748 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.17–2.23 (8H, m), 2.99–3.51 (4H, m), 4.00–4.11 (1H, m), 4.22, 4.23 (total 1H, d, *J*=8.4 Hz),

4.77, 4.79 (total 1H, d, J=8.4 Hz), 5.15, 5.37 (total 1H, d, J=4.3 Hz), 7.02–7.24 (10H, m).

NaH_2PO_4 (36 mg, 0.30 mmol), 2-methyl-2-butene (0.051 mL, 0.49 mmol), and $NaClO_2$ (18 mg, 0.15 mmol) were added to the solution of the above hemiacetal (60 mg, 0.99 mmol) in *tert*-BuOH/H_2O (v/v=5/1, 1.0 mL), and the mixture was stirred for 3 h at rt. HCl (10%) aqueous solution was added to the mixture and the solution was stirred for 3 h. The mixture was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by SiO_2 column chromatography (hexane/AcOEt=2/1 as an eluent) to give **13** (55 mg, 0.091 mmol, 92%). Colorless amorphous: $[\alpha]_D^{23.8}$ −32.1 (*c* 0.88, $CHCl_3$). IR (KBr): 3285, 1774, 1173, 912, 743 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.00 (1H, q, J=11.1 Hz), 1.15–1.54 (2H, m), 2.20–2.23 (1H, m), 2.50–2.66 (1H, m), 2.99–3.05 (2H, m), 3.10–3.82 (4H, m), 4.01–4.08 (1H, m), 4.17 (1H, d, J=8.4 Hz), 4.78 (1H, d, J=8.4 Hz), 7.21–7.98 (10H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 6.3, 32.5, 35.4, 38.2, 65.3, 76.9, 77.4, 78.4, 87.8, 127.0, 127.1, 127.9, 127.9, 128.0, 128.1, 128.3, 128.4, 128.5, 128.5, 128.6, 138.7, 178.0. Anal. Calcd for $C_{22}H_{24}I_2O_4$: C, 43.59; H, 3.99; I, 41.87. Found: C, 43.55; H, 4.03; I, 41.44.

*4.18. (3R,5R,2′S)-5-Iodomethyl-3-oxiranylmethyldihydrofuran-2-one (**14**)*

CAN (90 mg, 0.17 mmol) was added to a solution of **13** (50 mg, 0.083 mmol) in CH_3CN/H_2O (v/v=1/1, 0.8 mL). The mixture was stirred for 1 h at rt. After completion of the reaction (TLC check), H_2O was added to the mixture, which was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo to give the residue. Ag_2O (10 mg, 0.040 mmol) was added to a solution of the residue in CH_3CN (0.8 mL) under N_2 and the mixture was stirred for 3 h at 0–10 °C. Addition of AcOEt to the mixture formed precipitate, which was filtered through Celite pad. The filtrate was evaporated in vacuo to give the residue. The residue was purified by SiO_2 column chromatography (hexane/AcOEt=1/1 as an eluent) to give **14** (20 mg, 0.071 mmol, 86%). Colorless oil: $[\alpha]_D^{25.5}$ −9.7 (*c* 2.74, $CHCl_3$). IR (KBr): 1771, 1167, 912, 743 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.75 (1H, q, J=13.5 Hz), 1.88–1.92 (2H, m), 2.48–2.51 (1H, m), 2.67–2.94 (4H, m), 3.21–3.37 (1H, m), 3.38–3.42 (1H, m), 4.30–4.38 (1H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 6.6, 32.6, 35.5, 38.9, 46.9, 49.7, 76.8, 176.9. Anal. Calcd for $C_8H_{11}IO_3$: C, 34.06; H, 3.93; I, 44.99. Found: C, 34.07; H, 3.93; I, 44.66.

*4.19. (3R,5R,2′R)-3-(2-Hydroxydodec-11-enyl)-5-iodomethyldihydrofuran-2-one (**15a**)*

Grignard reagent (1.62 mL, 0.41 mmol, 0.25 M in Et_2O), prepared from 9-bromonon-1-ene[16] and Mg metal, was added to a solution of CuI (38 mg, 0.20 mmol) in Et_2O (0.8 mL) at −35 °C under N_2. The mixture was stirred for 30 min at the same temperature. Compound **14** (23 mg, 0.078 mmol) in Et_2O (0.5 mL) was added to the resulting solution and the mixture was stirred for additional 30 min at the same temperature. NH_4Cl aqueous solution was added to the mixture, which was extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, and evaporated in vacuo. The residue was purified by SiO_2 column chromatography (hexane/AcOEt=4/1 as an eluent) to give **15a** (20 mg, 0.049 mmol, 63%). Colorless oil: $[\alpha]_D^{21.3}$ +15.7 (*c* 0.35, $CHCl_3$). IR (KBr): 3416, 1759, 1186, 742 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.22–1.78 (16H, m), 1.89–2.00 (3H, m), 2.41–2.51 (1H, m), 2.78–2.91 (1H, m), 3.17–3.29 (3H, m), 3.62 (1H, br s, OH), 4.31–4.38 (1H, m), 4.84–4.95 (2H, m), 5.69–5.79 (1H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 14.8, 25.2, 28.9, 29.1, 29.3, 29.4, 29.4, 33.8, 35.4, 35.9, 37.1, 39.2, 69.6, 79.8, 114.1, 139.0, 179.5. Anal. Calcd for $C_{17}H_{29}IO_3$: C, 50.01; H, 7.16; I, 31.08. Found: C, 50.18; H, 6.98; I, 30.75.

*4.20. (3S,5R,2′R)-5-Dec-9-enyl-3-oxiranylmethyldihydrofuran-2-one (**16a**)*

K_2CO_3 (203 mg, 1.47 mmol) was added to a solution of **15a** (20 mg, 0.049 mmol) in AcOEt (0.6 mL). The mixture was stirred for 3 h at rt. After completion of the reaction (TLC check), AcOEt was added to the mixture and precipitate was filtered through Celite pad. The filtrate was concentrated in vacuo to give the residue. The residue was purified by SiO_2 column chromatography (hexane/AcOEt=4/1 as an eluent) to give **16a** (14 mg, 0.049 mmol, 100%). Colorless oil: $[\alpha]_D^{26.0}$ +29.8 (*c* 0.82, $CHCl_3$). IR (KBr): 1769, 1182, 912, 742 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.29–2.01 (19H, m), 2.50–2.59 (2H, m), 2.78–2.83 (2H, m), 2.99–3.02 (1H, m), 4.35–4.41 (1H, m), 4.92–5.03 (2H, m), 5.77–5.86 (1H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 25.2, 28.9, 29.0, 29.3, 29.4, 32.6, 33.8, 35.1, 35.4, 38.6, 46.8, 49.8, 77.2, 79.2, 114.1, 139.1, 178.1. Anal. Calcd for $C_{17}H_{28}O_3$: C, 72.82; H, 10.06. Found: C, 72.85; H, 10.10.

4.21. Rubrenolide

$Bi(OTf)_3$ (5 mg, 0.007 mmol) was added to a solution of **16a** (10 mg, 0.036 mmol) in THF/H_2O (v/v=4/1, 0.5 mL). The mixture was stirred under reflux for 6 h. After completion of the reaction (TLC check), K_2CO_3 was added to quench the acid. AcOEt was added to the mixture and the precipitate was filtered through Celite pad. The filtrate was concentrated in vacuo to give the residue. The residue was purified by SiO_2 column chromatography (hexane/AcOEt=1/2 as an eluent) to give rubrenolide (8 mg, 0.026 mmol, 73%). Colorless crystal: mp 98.0–100.0 °C. $[\alpha]_D^{24.7}$ +20.5 (*c* 0.29, $CHCl_3$). IR (KBr): 3310, 1747, 1190, 912, 742 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.27–2.03 (21H, m), 2.47–2.55 (1H, m), 2.86–2.93 (1H, m), 3.45–3.52 (1H, m), 3.60–3.65 (1H, m), 3.80–3.82 (1H, m), 4.38–4.42 (1H, m), 4.90–5.00 (2H, m), 5.75–5.84 (1H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 25.2, 28.9, 29.0, 29.3, 33.8, 35.3, 36.0, 39.5, 66.8, 70.6, 80.0, 114.1, 139.1, 180.4. LRMS (EI^+) *m/z* 298. HRMS (EI^+) Calcd for $C_{17}H_{30}O_4$: 298.2144. Found: 298.2141. The $[\alpha]_D$, ^1H and ^{13}C NMR, IR, and HRMS spectrum showed good agreement with those of authentic sample.

4.22. (3R,5R,2′R)-3-(2-Hydroxy-12-trimethylsilanyl-dodec-11-ynyl)-5-iodomethyldihydrofuran-2-one (**15b**)

In the same procedure for **15a**, **15b** (25 mg, 0.053 mmol, 50%) was obtained from Grignard reagent (1.3 mL, 0.64 mmol, 0.5 M in THF/TBME (v/v=1/1)), prepared from 9-bromo-1-trimethylsilylnon-1-yne[18] and Mg metal, CuI (61 mg, 0.32 mmol), and **14** (30 mg, 0.11 mmol) (SiO_2 column chromatography (hexane/AcOEt=4/1 as an eluent)). Colorless oil: $[\alpha]_D^{22.4}$ +13.1 (*c* 1.23, $CHCl_3$). IR (KBr): 3420, 1749, 1247, 748 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.12 (9H, s), 1.16–1.82 (17H, m), 1.94–2.00 (1H, m), 2.19 (1H, t, *J*=6.9 Hz), 2.50–2.55 (1H, m), 2.80–2.95 (1H, m), 3.22–3.34 (3H, m), 3.65 (1H, br s, OH), 4.31–4.90 (1H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 0.0 (3C), 14.5, 19.6, 24.9, 28.3, 28.5, 28.7, 29.0, 29.1, 35.1, 35.6, 36.8, 38.9, 69.3, 79.5, 84.0, 107.3, 179.2. Anal. Calcd for $C_{20}H_{35}IO_3Si$: C, 50.20; H, 7.37; I, 26.52. Found: C, 50.29; H, 7.21; I, 26.04.

4.23. (3S,5R,2′R)-3-Oxiranylmethyl-5-(10-trimethylsilanyl-dec-9-ynyl)dihydrofuran-2-one (**16b**)

In the same procedure for **16a**, **16b** (22 mg, 0.062 mmol, 99%) was obtained from K_2CO_3 (260 mg, 1.88 mmol) and **15b** (30 mg, 0.063 mmol) (SiO_2 column chromatography (hexane/AcOEt=4/1 as an eluent). Colorless oil: $[\alpha]_D^{24.3}$ +26.3 (*c* 0.76, $CHCl_3$). IR (KBr): 1773, 1180, 842 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.12 (9H, s), 1.23–1.98 (17H, m), 2.19 (2H, t, *J*=6.9 Hz), 2.48–2.57 (2H, m), 2.72–2.81 (2H, m), 2.96–2.99 (1H, m), 4.32–4.38 (1H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 0.0 (3C), 19.6, 25.1, 28.4, 28.5, 28.7, 29.1, 29.1, 32.4, 34.9, 35.2, 38.4, 46.6, 49.7, 79.0, 84.5, 107.5, 177.9. Anal. Calcd for $C_{20}H_{34}O_3Si$: C, 68.52; H, 9.78. Found: C, 68.42; H, 9.64.

4.24. Rubrynolide

$Bi(OTf)_3$ (13 mg, 0.02 mmol) was added to a solution of **16b** (33 mg, 0.094 mmol) in THF/H_2O (v/v=4/1, 0.9 mL). The mixture was stirred under reflux for 6 h. After completion of the reaction (TLC check), K_2CO_3 was added to quench the acid. AcOEt was added to the mixture and precipitate was filtered through Celite pad. The filtrate was concentrated in vacuo to give the residue. TBAF (1.0 M in THF, 0.14 mL, 0.14 mmol) was added to a solution of the obtained residue in THF (0.9 mL) under N_2 and the resulting solution was stirred for 30 min at rt. After completion of the reaction (TLC check), the reaction mixture was concentrated in vacuo to give the residue. The residue was purified by SiO_2 column chromatography (hexane/AcOEt=1/2 as an eluent) to give rubrynolide (19 mg, 0.066 mmol, 70%). Colorless crystal: mp 84.0–85.0 °C. $[\alpha]_D^{24.5}$ +21.0 (*c* 0.23, $CHCl_3$). IR (KBr): 3285, 1747, 913 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.19–1.80 (19H, m), 1.81–1.99 (2H, m), 2.01–2.12 (2H, m), 2.40–2.49 (1H, m), 2.80–2.86 (1H, m), 3.43 (1H, dd, *J*=9.5, 7.2 Hz), 3.57–3.60 (1H, m), 3.68–3.75 (1H, m), 4.28–4.38 (1H, m). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 18.4, 25.2, 28.4, 28.7, 29.0, 29.3, 29.3, 33.9, 35.4, 36.0, 39.3, 66.7, 68.1, 70.5, 79.9, 84.7, 180.2. LRMS (FAB) *m/z* 297 (MH^+). HRMS (FAB) Calcd for $C_{17}H_{29}O_4$: 297.2066. Found: 297.2089. The $[\alpha]_D$, ^1H and ^{13}C NMR, IR, and HRMS spectrum showed good agreement with those of authentic sample.

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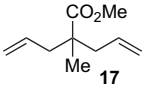

17

6. CCDC-244868 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336 033; or e-mail: deposit@ccdc.cam.ac.uk.
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