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Synthesis of (±)-Sundiversifolide Based on Lewis Acid-Mediated Claisen Rearrangement

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A new and concise synthesis of (±)-sundiversifolide (1), an allelopathic *bisnor*-sesquiterpene lactone isolated from germinating sunflower (*Helianthus annuus* L.) seeds, was achieved by employing Lewis acid-mediated Claisen rearrangement as the key step.

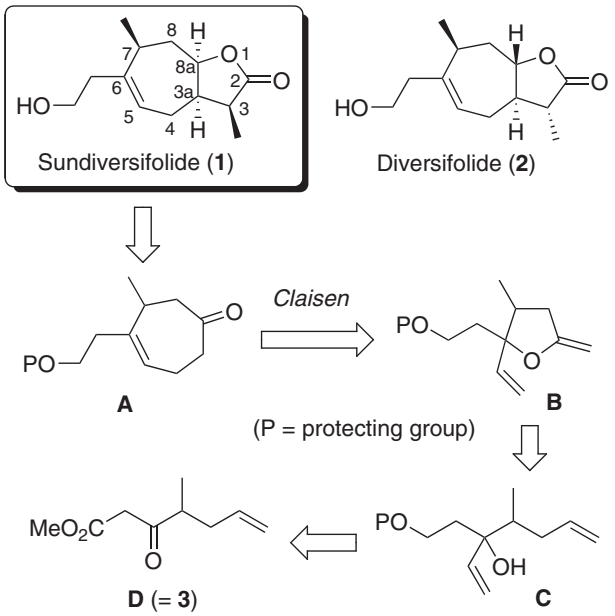
Key words: sundiversifolide; allelopathic agent; sesquiterpene; Claisen rearrangement

In 2001, Tomita-Yokotani *et al.* isolated a structurally interesting *bisnor*-xanthane sesquiterpene lactone from germinating sunflower (*Helianthus annuus* L.) seeds and named this lactone sundiversifolide.[1)] They have reported that sundiversifolide (**1**) showed unique allelopathic activities. In shoot and root growth tests of cat's-eyes (*Veronica persica* Poiret) seedlings, **1** promoted root growth at a concentration of 1 ppm, while it inhibited both shoot and root growth by *ca.* 50% at 30 ppm. This substance also showed interesting species-specificity in its plant growth-regulating effects on various tested plants.[1)] There exists one closely related natural product, that is diversifolide (**2**), which was isolated from *Tinthonia diversifolia* by Kuo and Lin.[2)] In respect of the chemical synthesis of **1**, Shishido *et al.* have recently disclosed the first enantioselective synthesis of (+)-**1**.[3)] However, the absolute configuration of naturally occurring **1** has remained unknown, because the specific rotation value of natural **1** has never been reported.

Inspired by its interesting biological activities and unique structure, we initiated synthetic studies on **1** in a continuation of our work on the syntheses of allelopathic agents.[4–6)] We report here a new and concise synthesis of (±)-**1**.

Results and Discussion

Our synthetic plan for **1** is illustrated in Scheme 1.



Scheme 1. Structure and Retrosynthetic Analysis of Sundiversifolide (**1**).

The target compound **1** should be obtainable from intermediate **A** *via* the construction of a butanolide moiety by regioselective installation of a propionate unit. To prepare **A**, we envisaged adopting a Lewis acid-mediated Claisen rearrangement as the key step. This key reaction may enable the desired 4-cycloheptenone framework to be concisely constructed from 2-methylene-5-vinyltetrahydrofuran derivative **B**. Key intermediate **B** would be preparable from acyclic precursor **C**. Thus, known β-ketoester **D** was assigned as an appropriate starting material.

The first step was the reduction of starting β-ketoester **3**[7)] (= **D**) to corresponding 1,3-diol **4**. Our first attempt to reduce **3** with $LiAlH_4$ was not successful, affording

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allylic alcohol **6** as the main product (31%), instead of desired diol **4** (23%). Although the formation of **6** was not expected in this case, this type of reaction has been reported as a useful method for the preparation of allylic alcohols and was intentionally performed by adding a base.[8] However, there was a need to optimize the reduction conditions. The second option was Soai's method, by which the reduction of β-ketoesters to the corresponding 1,3-diols has been successfully performed.[9,10] Although this gave desired diol **4** as the major product, the isolated yield was less than 40%. We thus turned to adopting a stepwise procedure. Reduction of **3** with $NaBH_4$ was followed by further reduction with $LiAlH_4$ to afford **4** in 89% yield.[11] Selective protection of a primary hydroxyl group of **4** as a TBDPS ether afforded **5** (89%). It was noted that the less expensive TBS protecting group was unable to survive under the conditions of the later iodoetherification. Oxidation of **5** with PDC furnished corresponding ketone **7** (88%), which was then treated with vinylmagnesium chloride to give alcohol **8** (= **C**; 97%) as a diastereomeric mixture. Iodoetherification of **8** was performed by the conventional manner to yield iodoether **9** (87%). Although yielded **9** was a complex mixture of all the possible stereoisomers, we were not concerned about this, because discussing diastereomeric isomerism was not the object of this exercise. A treatment with *t*-BuOK converted iodolactone **9** to key intermediate **10** (= **B**) which was used in the next key step without purification because of its instability.

The key 7-membered ring construction based on Claisen rearrangement was originally disclosed by Nozaki *et al.* in 1984.[12] They reported that Claisen rearrangement of 2-methylene-5-vinyltetrahydrofurans was successfully mediated by triisobutylaluminum (TIBAL) to furnish 4-cycloheptenols, which was derived from the initial Claisen adduct by successive reduction with aluminum hydride generated from TIBAL, in good to outstanding yield. We first examined the originally reported reaction conditions of TIBAL, CH_2Cl_2, $-78\,^{\circ}C$ to room temperature. However, desired adduct **11** was obtained in less than 40% yield based on **9**. Therefore, we changed the solvent from CH_2Cl_2 to toluene according to the other reports,[13,14] and the isolated yield was improved to 61%. Oxidation of **11** with PDC gave key 4-cycloheptenone **12** (= **A**; 87%).

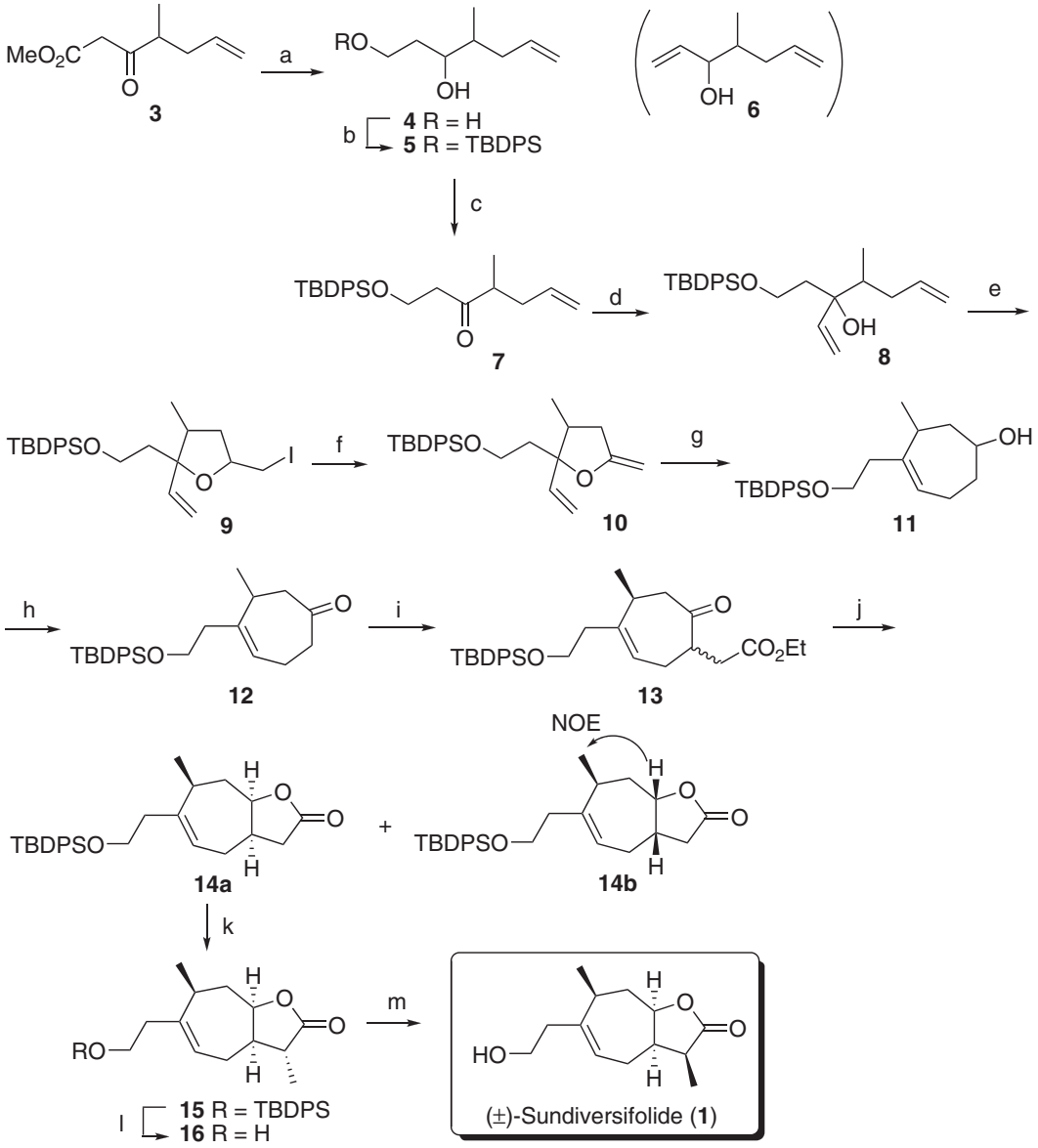
The remaining objective was to construct the α-substituted butanolide portion. One of the important points was the regioselective installation of a propionate unit. We first attempted a simple alkylation of the kinetically-controlled enolate anion of **12** with ethyl 2-bromopropanoate. However, the desired product could not be obtained, probably due to steric hindrance of the electrophile. We then turned our attention to the installation of an acetate unit. Ketone **12** was treated with LiHMDS and ethyl bromoacetate in the presence of HMPA at $-78\,^{\circ}C$ to furnish **13** as a diastereomeric mixture (α:β = *ca.* 1:1) in 78% yield with almost perfect regioselectivity. It was noteworthy that considerable amounts of regioisomers were yielded when the reaction was conducted without HMPA. Since this alkylation needed a higher temperature and longer time in the absence of HMPA, partial scrambling of the regiochemistry of the enolate anion might occur. It was also noted that the use of other bases such as LDA, KHMDS and NaHMDS had no positive effect on the isolated yield and diastereoselectivity. Obtained **13** was diastereoselectively reduced with L-Selectride® at $-78\,^{\circ}C$ to give a mixture of **14a** and **14b** which was purified by SiO_2 column chromatography to give pure **14a** (desired, 39%) and **14b** (undesired, 38%). Under these conditions, only *cis*-lactones (**14a**/**b**) were observed, while a considerable quantity of *trans*-lactones were obtained by reduction with $NaBH_4$ at $0\,^{\circ}C$ in MeOH. The relative configurations of **14a**/**b** were tentatively established by the observation of a NOE correlation in **14b**, as depicted in Scheme 2, and confirmed by the later conversion of **14a** into (±)-**1**. The spectral data for our synthetic **14a** are in good agreement with those reported by Shishido.[3] Although **14a** was known as the optically active form in Shishido's synthesis, we continued our synthesis of (±)-**1**. Methylation of **14a** was performed by treating with LiHMDS and MeI to give **15** as the sole product in 66% yield. Deprotection of the TBDPS group was achieved by treating with TBAF to give **16** (quant.). Finally, the α-oriented methyl group was successfully inverted by protonation of the dianion of **16** from the convex face to give a mixture of (±)-**1** and **16** (*ca.* 1:1). This mixture was chromatographically purified to give (±)-**1** [51%, (96% based on the recovered **16**)]. The various spectral data for synthetic (±)-**1** are in good accord with those of the natural product. The overall yield was 6.0% in 13 steps based on **3**.

In conclusion, a new and concise synthesis of (±)-sundiversifolide (**1**), an allelopathic substance isolated from sunflower seeds, was accomplished by starting from known ketoester **3**. A detailed bioassay employing our synthetic samples is now in preparation.

Experimental

IR spectra were measured with a Shimadzu IR-408 spectrometer, and ^{1}H-NMR spectra were recorded at 300 MHz with a Jeol JNM-AL300 spectrometer. The residual solvent peak in $CDCl_3$ (at $\delta_H = 7.26$) or CD_3OD (at $\delta_H = 3.30$) was used as the internal standard. ^{13}C-NMR spectra were recorded at 75 MHz with the Jeol JNM-AL300 spectrometer, the peak for $CDCl_3$ (at $\delta_C = 77.0$) or CD_3OD (at $\delta_C = 49.0$) being used as the internal standard. Mass spectra were measured with a Jeol JMS-SX102A spectrometer.

*4-Methyl-6-heptene-1,3-diol (**4**).* To a stirred solution of **3** (3.82 g, 22.4 mmol) in MeOH (60 ml) was added



Scheme 2. Synthesis of (±)-**1**.

Reagents and conditions: (a) i) $NaBH_4$, MeOH ii) $LiAlH_4$, THF (89%); (b) TBDPSCl, Et_3N, DMF (89%); (c) PDC, MS 4A, CH_2Cl_2 (88%); (d) vinylmagnesium chloride, THF (97%); (e) I_2, K_2CO_3, CH_3CN (87%); (f) *t*-BuOK, DMF; (g) TIBAL, toluene (61% in 2 steps); (h) PDC, MS 4A, CH_2Cl_2 (87%); (i) LiHMDS, $BrCH_2CO_2Et$, THF, HMPA, −78 °C (78%); (j) L-Selectride®, THF, −78 °C (39% for **14a**, 38% for **14b**); (k) LiHMDS, MeI, THF (66%); (l) TBAF, THF (quant.); (m) LiHMDS, NH_4Cl aq., THF (51% for **1**, 47% for **16**).

$NaBH_4$ (1.70 g, 44.8 mmol) at −10 °C. After stirring for 10 min, the reaction mixture was quenched with 6 N HCl and extracted with EtOAc. The organic layer was successively washed with water and brine, dried ($MgSO_4$), and concentrated under reduced pressure to give a crude product (3.50 g). To a stirred solution of this crude product (3.50 g) in THF (50 ml) was carefully added $LiAlH_4$ (2.56 g, 67.3 mmol) portionwise at 0 °C. After stirring for 10 min, the reaction mixture was quenched by the successive addition of water (2.6 ml), 1 N aq. NaOH, (2.6 ml) and then water (7.6 ml). This mixture was filtered, and the resulting filtrate was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed on SiO_2 to give **4** (2.88 g, 20.0 mmol, 89%) as an oil. It was noted that **4** was obtained as a mixture of the two possible diastereomers (*ca.* 1:1). IR ν_{max} (film) cm^{-1}: 3350 (s, O–H), 1645 (m, C=C). NMR δ_H ($CDCl_3$): 0.88 and 0.89 (total 3H, 2 × d, $J = 6.6$ Hz), 1.50–1.82 (3H, m), 1.82–1.99 (1H, m), 2.17–2.30 (1H, m), 2.92 (1H, s), 3.01 (1H, br s), 3.62–3.98 (3H, m), 4.97–5.07 (2H, m), 5.70–5.86 (1H, m). NMR δ_C ($CDCl_3$): 14.1, 14.5, 29.0, 29.4, 36.6, 36.8, 38.0, 38.3, 62.3, 62.5, 75.5, 75.9, 116.1, 116.3, 136.8, 136.9. HREIMS *m/z* $[M]^+$: calcd. for $C_8H_{16}O_2$, 144.1150; found, 144.1153.

1-(tert-Butyldiphenylsilyloxy)-4-methyl-6-hepten-3-ol (***5***). To a stirred solution of **4** (4.88 g, 33.8 mmol) in

CH_2Cl_2 (30 ml) were added Et_3N (4.45 g, 44.1 mmol) and TBDPSCl (10.2 g, 37.1 mmol). After stirring overnight at room temperature, the reaction mixture was diluted with water and extracted with hexane. The organic layer was successively washed with water and brine, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was chromatographed on SiO_2 to give **5** (11.5 g, 30.1 mmol, 89%) as an oil. IR ν_{max} (film) cm^{-1}: 3450 (s, O–H), 1640 (m, C=C). NMR δ_H ($CDCl_3$): 0.86 and 0.91 (total 3H, 2 × d, $J = 6.9$ Hz), 1.06 (9H, s), 1.54–1.82 (3H, m), 1.86–2.00 (1H, m), 2.24–2.36 (1H, m), 3.69–3.95 (3H, m) 4.97–5.09 (2H, m), 5.74–5.89 (1H, m), 7.37–7.48 (6H, m), 7.66–7.73 (4H, m). NMR δ_C ($CDCl_3$): 13.9, 15.0, 19.0, 26.8, 34.6, 35.5, 36.9, 37.5, 38.55, 38.60, 63.7, 63.8, 74.4, 75.4, 115.8, 127.8, 129.8, 133.0, 135.6, 137.6, 137.7. HREIMS m/z [M-^{t}Bu]$^+$: calcd. for $C_{20}H_{25}O_2Si$, 325.1622; found, 325.1617.

*1-(tert-Butyldiphenylsilyloxy)-4-methyl-6-hepten-3-one (**7**).* To a stirred solution of **5** (1.10 g, 2.88 mmol) in CH_2Cl_2 (10 ml) were added PDC (1.62 g, 4.31 mmol) and MS 4A (powdered; 2.0 g). After stirring for 5.5 h, the reaction mixture was filtered, and the resulting filtrate was concentrated under reduced pressure. The residue was chromatographed on SiO_2 to give **7** (970 mg, 2.55 mmol, 88%) as an oil. IR ν_{max} (film) cm^{-1}: 1720 (s, C=O). NMR δ_H ($CDCl_3$): 1.04 (9H, s), 1.09 (3H, d, $J = 6.9$ Hz), 2.03–2.14 (1H, m), 2.37–2.48 (1H, m), 2.57–2.73 (3H, m), 3.95 (2H, t, $J = 6.3$ Hz) 4.97–5.08 (2H, m), 5.66–5.79 (1H, ddt, $J = 17.1$, 9.9, 6.9 Hz), 7.36–7.47 (6H, m), 7.64–7.69 (4H, m). NMR δ_C ($CDCl_3$): 15.6, 19.1, 26.7, 36.7, 43.8, 46.5, 59.5, 116.7, 127.7, 129.6, 133.5, 135.5, 135.7, 212.3. HREIMS m/z [M-^{t}Bu]$^+$: calcd. for $C_{20}H_{23}O_2Si$, 323.1466; found, 323.1471.

*3-[2-(tert-Butyldiphenylsilyloxy)ethyl]-4-methyl-1,6-heptadien-3-ol (**8**).* To a stirred solution of **7** (2.57 g, 6.75 mmol) in THF (20 ml) was added vinylmagnesium chloride (1.47 M in THF; 9.18 ml, 13.5 mmol) at −15 °C under Ar. After stirring for 30 min, the reaction mixture was quenched with saturated aq. NH_4Cl and extracted with hexane. The organic layer was successively washed with water and brine, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was chromatographed on SiO_2 to give **8** (2.65 g, 6.48 mmol, 97%) as an oil. It was noted that **8** was obtained as a mixture of the two possible diastereomers (*ca.* 1:1). IR ν_{max} (film) cm^{-1}: 3500 (s, O–H), 1640 (w, C=C). NMR δ_H ($CDCl_3$): 0.86 and 0.94 (total 3H, 2 × d, $J = 6.9$ Hz), 1.05(10H, m), 1.52–1.89 (3H, m), 1.96–2.10 (1H, m), 2.36–2.60 (1H, m), 3.71–3.80 (1H, m), 3.86–3.96 (1H, m), 4.95–5.06 (2H, m), 5.26 and 5.28 (total 1H, 2 × dd, $J = 2.1$ Hz, 10.8 Hz), 5.46 and 5.49 (total 1H, 2 × dd, $J = 2.1$ Hz, 17.1 Hz), 5.68–5.85 (2H, m), 7.35–7.48 (6H, m), 7.65–7.74 (4H, m). NMR δ_C ($CDCl_3$): 13.0, 14.3, 18.7, 18.9, 25.6, 26.6, 26.7, 33.6, 35.1, 35.3, 36.1, 37.5, 38.3, 42.45, 42.50, 62.0, 62.1, 78.3, 78.4, 114.5, 114.6, 115.4, 115.5, 127.7, 127.8, 129.6, 129.9, 132.6, 134.8, 135.5, 135.6, 138.5, 138.7, 140.8, 141.9. HREIMS m/z [M-^{t}Bu]$^+$: calcd. for $C_{22}H_{27}O_2Si$, 351.1779; found, 351.1786.

*2-[2-(tert-Butyldiphenylsilyloxy)ethyl]-5-iodomethyl-3-methyl-2-vinyloxolane (**9**).* To a stirred solution of **8** (4.13 g, 10.1 mmol) in CH_3CN (30 ml) were added iodine (5.15 g, 20.4 mmol) and K_2CO_3 (4.19 g, 30.3 mmol) at 0 °C. After stirring for 1 h, the reaction mixture was quenched with 10% aq. $Na_2S_2O_3$ and extracted with ether. The organic layer was successively washed with water and brine, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was chromatographed on SiO_2 to give **9** (4.70 g, 8.79 mmol, 87%) as an oil. Although **9** was obtained as a complex mixture of the four possible diastereomers, the composition of these diastereomers was not carefully analyzed. IR ν_{max} (film) cm^{-1}: 1630 (w, C=C). NMR δ_H ($CDCl_3$): 0.93–1.01 (3H, m), 1.10–1.11 (9H, m), 1.10–2.35 (5H, m), 2.77–3.37 (2H, m), 3.74–4.06 (3H, m), 4.94–5.28 (2H, m), 5.62–5.80 (1H, m), 7.36–7.48 (6H, m), 7.65–7.75 (4H, m). NMR δ_C ($CDCl_3$, only clearly observed peaks): 9.3, 10.6, 13.4, 14.2, 14.3, 14.8, 19.1, 26.8, 26.9, 37.2, 37.8, 38.7, 40.2, 40.3, 41.3, 41.6, 42.2, 43.1, 44.1, 60.1, 60.3, 60.6, 76.5, 77.3, 77.6, 86.4, 87.2, 112.2, 112.9, 113.8, 114.2, 127.5, 129.5, 129.6, 133.9, 134.0, 135.5, 135.6, 138.2, 139.7, 141.6. HREIMS m/z [M-^{t}Bu]$^+$: calcd. for $C_{22}H_{26}O_2SiI$, 477.0746; found, 477.0740.

*2-[2-(tert-Butyldiphenylsilyloxy)ethyl]-3-methyl-5-methylene-2-vinyloxolane (**10**).* To a stirred solution of **9** (4.11 g, 7.69 mmol) in DMF (30 ml) was added *t*-BuOK (85%; 2.03 g, 15.4 mmol) at 0 °C. After stirring for 30 min, the reaction mixture was diluted with water and extracted with ether. The organic layer was successively washed with water and brine, dried (K_2CO_3), and concentrated under reduced pressure to give crude **10** (3.06 g). This was used in the next step without purification because of its instability. NMR δ_H ($CDCl_3$): 0.94 and 0.95 (total 3H, 2 × d, $J = 6.9$ Hz), 1.04 and 1.05 (total 9H, 2 × s), 1.60–2.77 (5H, m), 3.69–4.18 (4H, m), 4.94–5.36 (2H, m), 5.61 and 5.69 (total 1H, 2 × dd, $J = 17.1$, 10.8 Hz), 7.34–7.47 (6H, m), 7.64–7.75 (4H, m).

*4-[2-(tert-Butyldiphenylsilyloxy)ethyl]-3-methyl-4-cyclohepten-1-ol (**11**).* To a stirred solution of **10** (3.06 g) in toluene (30 ml) was added TIBAL (0.5 M in hexane; 30.8 ml, 15.4 mmol) at 0 °C. This solution was warmed to room temperature and stirred for 30 min. The reaction mixture was diluted with water, filtered, and the resulting filtrate was extracted with EtOAc. The organic layer was successively washed with water and brine, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was chromatographed on SiO_2 to give **11** (1.91 g, 4.67 mmol, 61%) as an oil. It was noted that

11 was obtained as a mixture of the two possible diastereomers (*ca.* 2:1). IR ν_{max} (film) cm^{-1}: 3400 (s, O–H). NMR δ_H ($CDCl_3$): 0.99–1.10 (12H, m), 1.10–2.40 (10H, m), 3.62–4.03 (3H, m), 5.41–5.53 (1H, m), 7.34–7.46 (6H, m), 7.65–7.72 (4H, m). NMR δ_C ($CDCl_3$): 14.1, 17.4, 19.2, 19.8, 22.3, 22.6, 26.9, 31.5, 31.8, 33.8, 35.2, 36.9, 38.0, 41.9, 42.4, 43.7, 63.4, 64.2, 70.2, 73.9, 126.2, 126.7, 127.6, 129.5, 134.0, 135.6, 143.1. HREIMS *m/z* $[M\text{-}^tBu]^+$: calcd. for $C_{22}H_{27}O_2Si$, 351.1779; found, 351.1776.

*4-[2-(tert-Butyldiphenylsilyloxy)ethyl]-3-methyl-4-cyclohepten-1-one (**12**).* To a stirred solution of **11** (4.00 g, 9.79 mmol) in CH_2Cl_2 (50 ml) were added PDC (5.52 g, 14.7 mmol) and MS 4A (powdered; 6.0 g). After stirring for 6 h, the reaction mixture was filtered, and the resulting filtrate was concentrated under reduced pressure. The residue was chromatographed on SiO_2 to give **12** (3.46 g, 8.50 mmol, 87%) as an oil. IR ν_{max} (film) cm^{-1}: 1710 (s, C=O). NMR δ_H ($CDCl_3$): 1.01 (3H, d, $J = 6.6$ Hz), 1.05 (9H, s), 2.17–2.34 (4H, m), 2.34–2.48 (4H, m), 2.81 (1H, dd, $J = 3.6$ Hz, 12.0 Hz), 3.71 (2H, t, $J = 6.9$ Hz), 5.55 (1H, t, $J = 6.0$ Hz), 7.35–7.45 (6H, m), 7.64–7.68 (4H, m). NMR δ_C ($CDCl_3$): 19.1, 19.3, 22.7, 26.8, 34.3, 40.5, 43.6, 48.5, 63.4, 125.1, 127.6, 129.6, 133.8, 135.5, 142.6, 213.0. HREIMS *m/z* $[M\text{-}^tBu]^+$: calcd. for $C_{22}H_{25}O_2Si$, 349.1621; found, 349.1616.

*Ethyl 2-{4-[2-(tert-butyldiphenylsilyloxy)ethyl]-5-methyl-7-oxo-3-cyclohepten-1-yl}acetate (**13**).* LiHMDS (1.6 M in THF; 1.9 ml, 3.0 mmol) was added to dry THF (5 ml) under Ar at −78 °C. To this solution, **12** (880 mg, 2.16 mmol) in THF (5 ml) was slowly added dropwise. After stirring for 40 min, HMPA (0.83 ml, 4.8 mmol) and $BrCH_2CO_2Et$ (0.57 ml, 4.7 mmol) were added dropwise, and the mixture was stirred for 20 min. The reaction mixture was quenched with saturated aq. NH_4Cl at −78 °C and then extracted with EtOAc. The organic layer was successively washed with water and brine, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was chromatographed on SiO_2 to give **13** (835 mg, 1.68 mmol, 78%) as an oil. IR ν_{max} (film) cm^{-1}: 1740 (s, C=O), 1710 (s, C=O). NMR δ_H ($CDCl_3$): 0.96 (3H, d, $J = 6.9$ Hz), 1.05–1.06 (9H, m), 1.24 and 1.25 (total 3H, 2 × t, $J = 7.2$ Hz), 1.97–2.99 (10H, m), 3.71 and 3.74 (total 2H, 2 × t, $J = 6.9$ Hz), 4.12 and 4.13 (total 2H, 2 × q, $J = 7.2$ Hz), 5.49–5.58 (1H, m), 7.35–7.46 (6H, m), 7.65–7.70 (4H, m). NMR δ_C ($CDCl_3$): 14.0, 14.1, 17.6, 19.08, 19.11, 19.6, 26.8, 28.4, 28.9, 34.0, 34.6, 35.6, 35.9, 39.8, 41.9, 47.3, 48.0, 49.1, 49.4, 60.4, 63.1, 63.4, 123.5, 123.8, 127.6, 133.7, 135.5, 142.7, 144.3, 172.2, 172.4, 211.6, 212.0. HREIMS *m/z* $[M]^+$: calcd. for $C_{30}H_{40}O_4Si$, 492.2696; found, 492.2690.

(3aR,7S*,8aR*)-6-[2-(tert-Butyldiphenylsilyloxy)ethyl]-7-methyl-3,3a,4,7,8,8a-hexahydrocyclohepta[2,1-b]furan-2-one (**14a**) and (3aS*,7S*,8aS*)-6-[2-(tert-butyldiphenylsilyloxy)ethyl]-7-methyl-3,3a,4,7,8,8a-hexahydrocyclohepta[2,1-b]furan-2-one (**14b**).* To a stirred solution of **13** (295 mg, 0.592 mmol) in THF (10 ml) was added L-Selectride® (1.02 M in THF; 1.17 ml, 1.19 mmol) at −78 °C under Ar. After stirring for 10 min, the reaction mixture was quenched with saturated aq. NH_4Cl and extracted with EtOAc. The organic layer was successively washed with water and brine, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was chromatographed on SiO_2 to give **14a** (103 mg, 0.229 mmol, 39%) and **14b** (102 mg, 0.228 mmol, 38%).

14a: IR ν_{max} (film) cm^{-1}: 1780 (s, C=O). NMR δ_H ($CDCl_3$): 1.05–1.08 (12H, m), 1.89–2.42 (8H, m) 2.60 (1H, dd, $J = 9.0$ Hz, 17.7 Hz), 2.71–2.85 (1H, m), 3.69 (2H, t, $J = 6.9$ Hz), 4.57 (1H, dd, $J = 8.1$, 14.7 Hz), 5.38 (1H, dd, $J = 5.1$ Hz, 8.7 Hz), 7.36–7.47 (6H, m), 7.64–7.69 (4H, m). NMR δ_C ($CDCl_3$): 19.1, 20.8, 26.8, 27.4, 34.5, 34.7, 35.6, 37.3, 39.5, 63.2, 81.4, 122.1, 127.6, 129.6, 133.7, 135.48, 135.51, 142.5, 176.6. HREIMS *m/z* $[M\text{-}^tBu]^+$: calcd. for $C_{24}H_{27}O_3Si$, 391.1727; found, 391.1722.

14b: Mp 98–101 °C. IR ν_{max} (nujol) cm^{-1}: 1780 (s, C=O). NMR δ_H ($CDCl_3$): 1.03–1.06 (12H, m), 1.84 (1H, m), 2.07–2.46 (7H, m), 2.63–2.74 (1H, m), 2.82 (1H, dd, $J = 8.7$ Hz, 17.4 Hz), 3.68 (2H, t, $J = 6.9$ Hz), 4.79 (1H, dd, $J = 7.8$ Hz, 14.4 Hz), 5.33 (1H, dd, $J = 3.0$ Hz, 8.4 Hz), 7.35–7.46 (6H, m), 7.64–7.68 (4H, m). NMR δ_C ($CDCl_3$): 18.5, 19.1, 26.8, 28.7, 33.8, 34.1, 37.2, 39.0, 39.5, 63.5, 80.9, 123.0, 127.6, 129.6, 133.79, 133.83, 135.5, 143.7, 176.6. HREIMS *m/z* $[M\text{-}^tBu]^+$: calcd. for $C_{24}H_{27}O_3Si$, 391.1727; found, 391.1724.

(3R,3aR*,7S*,8aR*)-6-[2-(tert-Butyldiphenylsilyloxy)-ethyl]-3,7-dimethyl-3,3a,4,7,8,8a-hexahydrocyclohepta-[2,1-b]furan-2-one (**15**).* LiHMDS (1.6 M in THF; 0.365 ml, 0.584 mmol) was added to dry THF (2 ml) under Ar at −78 °C. To this solution, **14a** (187 mg, 0.417 mmol) in THF (1 ml) was slowly added dropwise. After stirring for 1 h, MeI (0.042 ml, 0.63 mmol) was added dropwise, and the mixture was stirred for 15 min. The reaction mixture was quenched with saturated aq. NH_4Cl and extracted with hexane. The organic layer was successively washed with water and brine, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was chromatographed on SiO_2 to give **15** (127 mg, 0.274 mmol, 66%) as an oil. IR ν_{max} (film) cm^{-1}: 1770 (s, C=O). NMR δ_H ($CDCl_3$): 1.05–1.07 (12H, m), 1.21 (3H, d, $J = 6.6$ Hz), 1.78–2.42 (9H, m), 3.66–3.74 (2H, m), 4.40–4.48 (1H, m) 5.38 (1H, dd, $J = 5.4$ Hz, 8.4 Hz), 7.36–7.47 (6H, m), 7.65–7.68 (4H, m). NMR δ_C ($CDCl_3$): 13.9, 19.1, 20.5, 26.3, 26.8, 35.1, 35.3, 39.2, 39.5, 45.0, 63.3, 79.2, 121.1, 127.6, 129.6, 133.7, 135.5, 142.8, 179.4. HREIMS *m/z* $[M\text{-}^tBu]^+$: calcd. for $C_{25}H_{29}O_3Si$, 405.1884; found, 405.1880.

(3R,3aR*,7S*,8aR*)-6-(2-Hydroxyethyl)-3,7-dimethyl-3,3a,4,7,8,8a-hexahydrocyclohepta[2,1-b]furan-2-one*

*(**16**).* To a stirred solution of **15** (12 mg, 0.026 mmol) in THF (1 ml) was added TBAF (1.0 M in THF; 0.026 ml, 0.026 mmol). After stirring for 1 h, the reaction mixture was quenched with saturated aq. NH_4Cl and extracted with EtOAc. The organic layer was successively washed with water and brine, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was chromatographed on SiO_2 to give **16** (6.0 mg, quant.). IR ν_{max} (film) cm^{-1}: 3400 (s, O–H), 1760 (s, C=O). NMR δ_H ($CDCl_3$): 1.16 (3H, d, J = 6.9 Hz), 1.23 (3H, d, J = 6.9 Hz), 1.54 (1H, br s), 1.82–2.09 (2H, m), 2.10–2.50 (7H, m), 3.59–3.72 (2H, m), 4.44–4.53 (1H, m), 5.48 (1H, dd, J = 5.4, 8.4 Hz). NMR δ_C ($CDCl_3$): 13.9, 20.6, 26.3, 35.1, 35.2, 39.2, 39.5, 45.0, 61.0, 79.1, 121.7, 142.3, 179.4. HRFABMS m/z $[M+H]^+$: calcd. for $C_{13}H_{21}O_3$, 225.1490; found, 225.1489.

(3S,3aR*,7S*,8aR*)-6-(2-Hydroxyethyl)-3,7-dimethyl-3,3a,4,7,8,8a-hexahydrocyclohepta[2,1-b]furan-2-one: (±)-sundiversifolide (**1**).* LiHMDS (1.6 M in THF; 0.047 ml, 0.075 mmol) was added to dry THF (2 ml) under Ar at −78 °C. To this solution, **16** (7.0 mg, 0.031 mmol) in THF (1 ml) was slowly added dropwise. After stirring for 1 h, the reaction mixture was quenched with saturated aq. NH_4Cl and extracted with EtOAc. The organic layer was successively washed with water and brine, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was chromatographed on SiO_2 to give (±)-sundiversifolide (**1**) [3.6 mg, 0.016 mmol, 51% (96% based on the recovered **16**)] and recovered **16** (3.3 mg, 0.015 mmol, 47%) as an oil. IR ν_{max} (film) cm^{-1}: 3400 (s, O–H), 1760 (s, C=O). NMR δ_H (CD_3OD): 1.11 (3H, d, J = 7.5 Hz), 1.15 (3H, d, J = 7.2 Hz), 1.85–1.95 (1H, m), 1.98–2.05 (2H, m), 2.08–2.25 (2H, m), 2.30–2.45 (2H, m), 2.70–2.81 (1H, m), 2.85–2.95 (1H, m), 3.49–3.65 (2H, m), 4.65–4.74 (1H, m), 5.53–5.56(1H, m). NMR δ_C (CD_3OD): 11.0, 21.9, 22.9, 34.0, 38.2, 40.2, 41.2, 43.6, 62.2, 82.5, 125.4, 143.6, 181.9. HRFABMS m/z $[M+H]^+$: calcd. for $C_{13}H_{21}O_3$, 225.1490; found, 225.1487.

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