有机化学 DOI: 10.6023/cjoc202101049 研究论文
Chinese Journal of Organic Chemistry ARTICLE

3-芳基-7-甲基-7-羟基-2-辛烯-6-内酯类化合物的合成及杀菌活性

王卫伟 赵 宇 刘鑫磊 蒋家珍 王明安*
(中国农业大学应用化学系 农药创新研究中心 北京 100193)

摘要 为了优化3-苯基-7-甲基-7-羟基-2-辛烯-6-内酯的化学结构, 通过环氧化-内酯化和Sharpless不对称双羟基化反应作为关键步骤, 分别以61%～91%的收率实现了消旋及光活性3-芳基-7-甲基-7-羟基-2-辛烯-6-内酯类化合物的合成, 其结构经过IR, ^{1}H NMR, ^{13}C NMR和HR-ESI-MS的表征. 对它们的杀菌活性进行了评价, 结果表明(*R*)-3-苯基-7-甲基-7-羟基-2-辛烯-6-内酯(**5a**)活性最好的化合物, 对6种植物病原菌的EC_{50}值在0.2～13.5 μg/mL范围, 优于其(*S*)-异构体及消旋体混合物. 它可以作为先导结构进行进一步结构优化. 扫描电镜和透射电镜观测的结果显示, 化合物(*S*)-**5a**, **5d** 和 **5j** 对油菜菌核菌菌丝细胞的结构和功能有显著影响.

关键词 3-芳基-7-甲基-2-辛烯-6-内酯; 环氧化-内酯化反应; 不对称双羟基化反应; 杀菌活性

Synthesis and Antifungal Activity of 3-Aryl-7-methyl-7-hydroxy-2-octen-6-olide

Wang, Weiwei Zhao, Yu Liu, Xinlei Jiang, Jiazhen Wang, Ming'an*
(*Innovation Center of Pesticide Research*, *Department of Applied Chemistry*, *China Agricultural University*, *Beijing 100193*)

Abstract In order to optimize the structure of 3-phenyl-7-methyl-7-hydroxy-2-octen-6-olide, the synthesis of racemic and optical 3-aryl-7-methyl-7-hydroxy-2-octen-6-olides has been achieved via epoxidation-lactonization procedure and Sharpless asymmetric dihydroxylation as the key steps in 61%～91% yields, respectively. Their structures were fully characterized by IR, ^{1}H NMR, ^{13}C NMR, and HRMS data. Their antifungal activities were evaluated, and it showed that (*R*)-3-phenyl-7-methyl-7-hydroxy-2-octen-6-olide (**5a**) was the most active compound with the EC_{50} values in the range of 0.2～13.5 μg/mL against the tested six phytopathogens, better than its (*S*)-isomer and racemic mixture. It would be the potential lead structure to be optimized. The scanning electron microscopy (SEM) and transmission electron microscopy (TEM) observation indicated that compounds (*S*)-**5a**, **5d** and **5j** had a significant impact on the structure and function of the hyphal cell wall of *S. sclerotiorum* mycelium.

Keywords 3-aryl-7-methyl-7-hydroxy-2-octen-6-olide; epoxidation-lactonization; asymmetric dihydroxylation; antifungal activity

1 Introduction

3,7-Dimethyl-7-hydroxy-2-octen-6-olide (**1**) is a naturally occurring seven-membered lactone that was isolated from the honey bee fungal entomopathogen *Ascosphaera apis*, as well as the fruit of plant *Litsea cubeba* in Tibet. It exhibited good antifungal and antioxidant activities.[1-2] As reported in literature, the lactone motif plays an important role in the chemical communication between wide varieties of organisms,[3] and this class of naturally occurring lactones was confirmed to have a wide range of biological properties such as antifungal, antimicrobial, and phytotoxic activities as well as cytotoxicity against human tumour cells.[4-7] These interesting structures and promising biological profiles have attracted significant attention from a number of researchers, and several interesting synthetic strategies for these compounds have been reported and reviewed.[3,8-13] However, the natural products with seven-membered lactone have rarely been reported and synthesized in the literatures (Figure 1, **1**～**4**),[14-22] because they have a unique ring strain seven-membered lactone structure, and the synthesis of them is practically challenged.[23-29] In the previous paper, we paid our attention to

* Corresponding author. E-mail: wangma@cau.edu.cn
Received January 28, 2021; revised February 24, 2021; published online March 19, 2021.
Project supported by the National Natural Science Foundation of China (Nos. 21772229, 21172254) and the National Hi-Tech R & D Program of China (No. 2011AA10A202).
国家自然科学基金(Nos. 21772229, 21172254)和国家高科技研发计划(No. 2011AA10A202)资助项目.

the total synthesis of natural products with seven membered lactone moiety and their biological activities, the synthesis and biological activity evaluation of the racemic 3,7-dimethyl-7-hydroxy-2-octen-6-olide (**1**), 3,7-dimethyl-2,6-octadien-1,6-olide (**2**), 7-methyl-7-hydroxy-2-octen-6-olide (**5**), and their 3-(2-hydroxypropan-2-yl)-4,5-dihydrobenzo[*c*]oxepin-1-(3*H*)-one analogues (**6**) were carried out in our laboratory.[30-33] 3-Phenyl-7-methyl-7-hydroxy-2-octen-6-olide (**5a**, R＝Ph) was found to exhibit much excellent fungicidal activities against several phytopathogens than naturally occurring 3,7-dimethyl-7-hydroxy-2-octen-6-olide (**1**) and the other derivatives. However, the optical isomers of **5a** were not prepared because the key intermediate (*E*)- and (*Z*)-configuration mixtures of Wittig reaction products were obtained with about 18%～20% desired (*E*)-configuration isomer and not purified.[33] In order to optimize the structure of 3-phenyl-7-methyl-7-hydroxy-2-octen-6-olide and compare the differences of the optical isomers of **5a** based on the above results, the synthesis of racemic and optical lactones **5** with different aryl groups by Mizoroki-Heck arylation, epoxidation-lactonization approaches and Sharpless asymmetric dihydroxylation were explored, and their antifungal activity evaluation was reported in this paper.

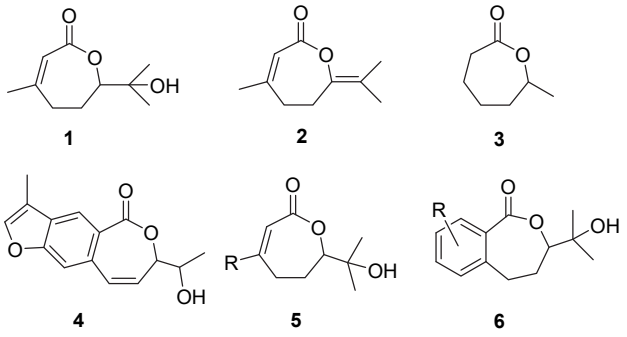


Figure 1 Representing naturally occurring and synthesized seven-membered lactones in references[2]

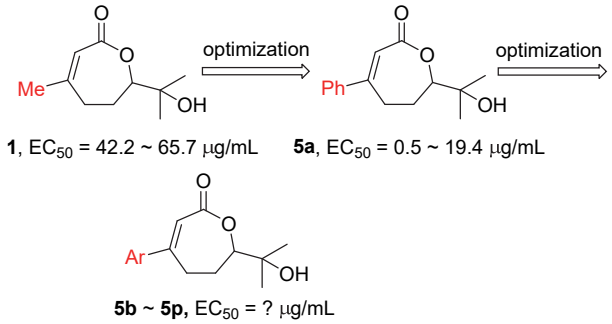
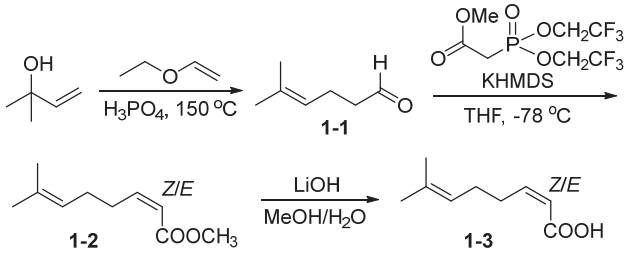


Figure 2 Optimization strategy of seven-membered lactones in this paper

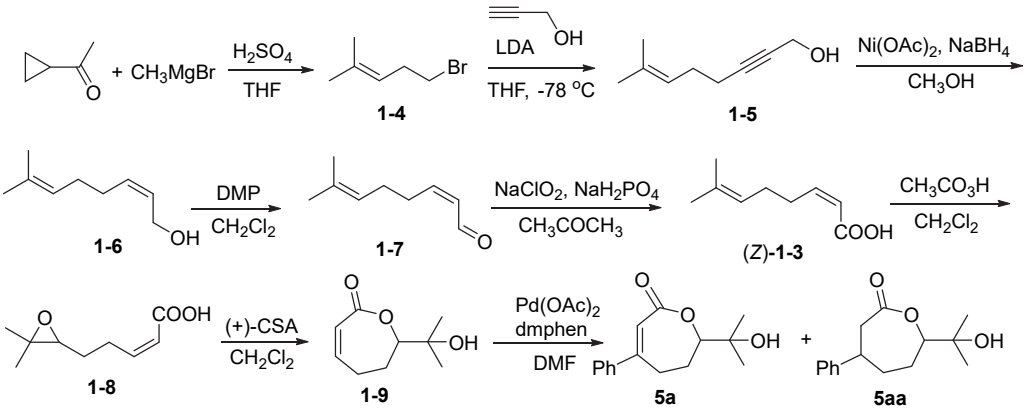
2 Results and discussion

The synthesis of racemic 3-aryl-7-methyl-7-hydroxy-2-octen-6-olides **5** was redesigned using acid (*Z*)-**1-3** as the starting material and epoxidation-lactonization as the key step as in the previous paper.[30-33] In an effort to promote the application of this epoxidation-lactonization procedure and obtain the aryl analogues **5** of **1**, three-step strategy of preparing **1-3** was initially utilized. The compound **1-1** was synthesized in 50% yield (Scheme 1), the Wittig reaction was carried out to produce the mixture of (*Z*)- and (*E*)-**1-2**, the mixture of (*Z*)- and (*E*)-**1-3** was prepared from ester **1-2** by LiOH hydrolyzation.[34-35] However, the quantity of (*Z*)-**1-2** and (*Z*)-**1-3** were still only 18%～20% in these mixtures, and difficult to purify them. So this route was given up. After through five-step reaction exploration in Scheme 2, the high purity of (*Z*)-**1-3** was obtained, and the seven-membered lactone **1-9** was afforded by the epoxidation-lactonization protocol in high overall yield (Scheme 2). However, the Heck reaction of lactone **1-9** with phenyl boronic acid provided the mixture of **5a** and **5aa**, which were not separated by column chromatography and preparation HPLC. So the strategy of preparing racemic and optical lactones **5** was unsuccess using epoxidation-lactonization of olefin acid (*Z*)-**1-3** and Heck reaction of lactone **1-9** as the key steps. After examining the references and repeated experiments, the compound **1-1** was prepared in high yield (Scheme 3). Then single ester (*E*)-**1-12** was obtained through Wittig reaction, the olefin acid (*E*)-**1-3** was prepared by LiOH hydrolyzation in 96% yield. When (*E*)-**1-3** was in hand, the Mizoroki-Heck arylation of (*E*)-**1-3** with aryl iodide catalyzed by $Pd(OAc)_2$ and $P(o\text{-}MeC_6H_4)_3$ was carried out to afford the olefin acids (*E*)-**1-13** in good yields in the previous report,[36] which was epoxidized by peracetic acid to give epoxides **1-14**. The epoxide **1-14** was cyclized to afford the seven-membered lactone compounds **5** in the presence of catalyst (＋)-camphorsulfonic acid (CSA) in 61%～91% overall yields for two steps (Table 1, Entries 1～19).[33]

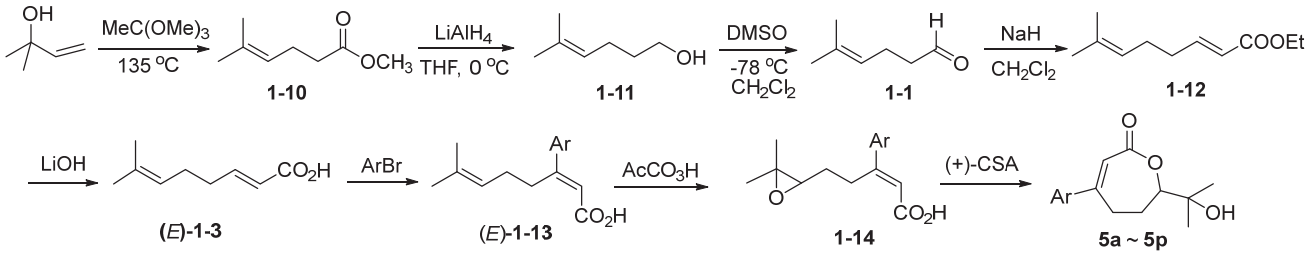


Scheme 1 Synthesis of olefin acid (*E*/*Z*)-**1-3**

In order to get insights into the structure-activity relationship of this kind of compounds, some representing compounds which exhibited 70% antifungal activities in the preliminary screen were selected to prepare their optical isomers. First, (*E*)-**1-13a** was esterified with methanol to provide ester **15a**, subsequent dihydroxylation of compound **15a** with AD-mix-*β* gave compound **16a** in 84% yield and 98.7% *ee*. After removal of the methyl group by LiOH hydrolyzation at room temperature to give chiral diol acid **20a**, the chiral acid **20a** was treated with 2,4,6-trichlorobenzoyl chloride (2,4,6-TCBC) via Yama-



Scheme 2 Synthesis of **5a** and **5aa** by epoxidation-lactonization and Heck reaction



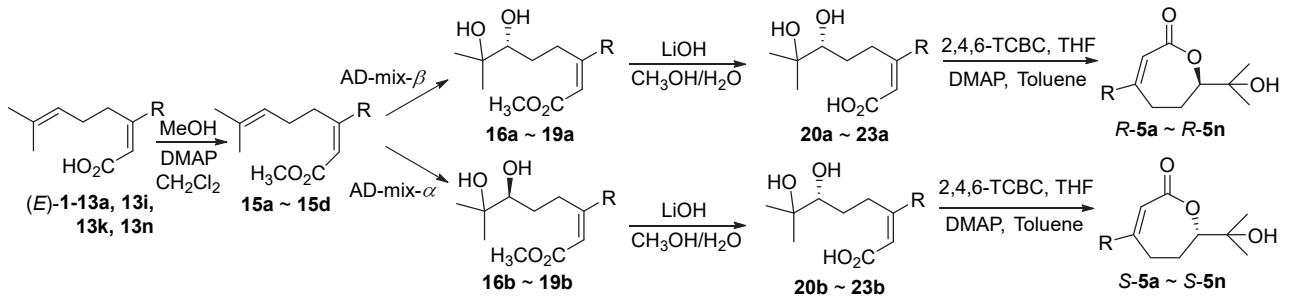
Scheme 3 Synthesis of racemic seven-membered lactones **5** by epoxidation-lactonization

Table 1 Synthesis of seven-membered lactones **5** via epoxidation-lactonization strategy

Entry	Ar	Olefin acid	Lactone	Yield/%
1	C_6H_5	**1-13a**	**5a**	80
2	2-ClC_6H_4	**1-13b**	**5b**	91
3	3-ClC_6H_4	**1-13c**	**5c**	84
4	4-ClC_6H_4	**1-13d**	**5d**	69
5	4-$CH_3OC_6H_4$	**1-13e**	**5e**	61
6	4-$CH_3C_6H_4$	**1-13f**	**5f**	75
7	4-FC_6H_4	**1-13g**	**5g**	70
8	4-$CF_3C_6H_4$	**1-13h**	**5h**	81
9	4-PhC_6H_4	**1-13i**	**5i**	82
10	1-$C_{10}H_7$	**1-13j**	**5j**	73
11	2-$C_{10}H_7$	**1-13k**	**5k**	84
12	4-$CH_3COC_6H_4$	**1-13l**	**5l**	68
13	4-$CH_3O_2CC_6H_4$	**1-13m**	**5m**	78
14	4-$(CH_3)_3CC_6H_4$	**1-13n**	**5n**	90
15	4-CNC_6H_4	**1-13o**	**5o**	65
16	2-$CH_3OC_6H_4$	**1-13p**	**5p**	88
17	2-$CH_3C_6H_4$	**1-13q**	**5q**	81
18	2,4-$(CH_3)_2C_6H_4$	**1-13r**	**5r**	79
19	3,5-$(CH_3)_2C_6H_4$	**1-13s**	**5s**	85

guchi reaction in THF, then the mixture was heated in toluene to successfully produce the lactone *R*-**5a** in 81% yield with 96.5% *ee*.[33] The enantiomer *S*-**5a** was also preparred by the same procedure with AD-mix-*α* replacing AD-mix-*β* in 75% yield with 94.1% *ee* through ester **16b** and chiral acid **20b**. After *R*-**5a** and *S*-**5a** were obtained, the 4-PhC_6H_4, 4-*t*-$C_4H_9C_6H_4$ and 2-$C_{10}H_7$ analogues (*R*-**5i** and *S*-**5i**, *R*-**5k** and *S*-**5k**, *R*-**5n** and *S*-**5n**) were also synthesized in the similar approaches (Scheme 4). (*E*)-Methyl 3-aryl-7-methyl-octa-2,6-dienoate **15b**～**15d** were transformed to chiral diol esters intermediates **17a**～**19a** and 17**b**～**19b** under Sharpless asymmetric dihydroxylation condition. Then LiOH hydrolyzation of chiral diol esters **17a** and **17b** and Yamaguchi reaction of chiral diol acids **21a** and **21b** were used to afford the compounds *R*-**5i** and *S*-**5i** in 66% and 67% yields with *ee* values of 98.0% and 94.1%. Compounds *R*-**5k** and *S*-**5k** from chiral diol esters **18a** and **18b** via chiral diol acids **22a** and **22b** in 86% and 91% yields with *ee* values of 95.0% and 97.7%, compounds *R*-**5n** and *S*-**5n** from chiral diol esters **19a** and **19b** via chiral diol acids **23a** and **23b** in 69% and 72% yields with *ee* values of 98.1% and 95.2% were prepared in a similar approach, respectively.

The *in vitro* antifungal activities of synthesized seven-membered lactone were evaluated using the mycelial growth rate test at (25±0.5) ℃ following the protocol in reference,[33,37-39] Chlorothalonil and carbendazim used as positive control, and the EC_{50} values were determined from the inhibition rates of five different concentrations for the compounds having more than 70% inhibition rates, which were given in Table 2. The data showed that most of the synthesized seven-membered lactones have significant antifungal activities against these phytopathogens with EC_{50} values of 0.6～150.8 μg/mL. From these data, we found that the lactones **5a**, **5i**, **5k** and **5n** were more active than the other lactones **5b**～**5p** against *R. solani*, *A. solani*, *S. sclerotiorum*, *B. cinerea*, *F. graminearum* and *P. capsici*, only lactone **5a** exhibited antifungal activities against *A.*



13a, **15a**, **16a**, **16b**, **20a**, **20b**, *R*- and *S*-**5a**: R = Ph; **13i**, **15b**, **17a**, **17b**, **21a**, **21b**, *R*- and *S*-**5i**: R = 4-PhC_6H_4

13k, **15c**, **18a**, **18b**, **22a**, **22b**, *R*- and *S*-**5k**: R = 4-*t*-$C_4H_9C_6H_4$; **13n**, **15d**, **19a**, **19b**, **23a**, **23b**, *R*- and *S*-**5n**: R = 2-$C_{10}H_7$

Scheme 4 Synthesis of *R*-**5a**～*R*-**5n** and *S*-**5a**～*S*-**5n** by Sharpless asymmetric dihydroxylation

Table 2 EC_{50} (μg/mL) values for antifungal activity of synthesized seven-membered lactones **5**

Compd.	*R. solani*	*A. solani*	*S. sclerotiorum*	*B. cinerea*	*F. graminearum*	*P. capsici*
5a	10.7	3.7	5.1	0.5	19.4	18.6
R-**5a**	4.6	2.4	2.8	0.2	13.5	12.0
S-**5a**	15.5	9.8	10.4	1.4	26.2	25.7
5d	—[a]	—	12.3	—	—	—
5i	35.9	—	37.5	11.3	—	35.0
R-**5i**	12.6	—	13.3	9.7	—	17.9
S-**5i**	62.8	—	68.6	24.5	—	65.3
5j	—	—	12.8	—	—	—
5k	104.0	—	11.6	23.7	—	40.0
R-**5k**	64.5	—	4.8	8.6	—	22.7
S-**5k**	150.8	—	24.4	35.8	—	68.2
5n	54.1	—	15.2	—	—	57.6
R-**5n**	38.2	—	8.3	—	—	22.1
S-**5n**	84.5	—	30.8	—	—	88.6
Carbendazim	0.05	0.05	7.9	528.2	0.07	77.8

[a] "—" Indicated that the EC_{50} values were not determined due to weak inhibitory activities.

solani and *F. graminearum*. Comparison the structures of **5a**～**5p**, we found that **5a** and the compounds having 4-(*t*-butyl)phenyl (**5n**), 4-phenylphenyl (**5i**), 1-naphthyl (**5j**) and 2-naphthyl (**5k**) at the 3-position of lactone exhibited much higher activities than that of the other substitutent groups at the 3-position of lactone. In the other aspect, The *R*-isomers of **5a**, **5i**, **5k** and **5n** had much higher activities than that of the racemic and *S*-isomers of **5a**, **5i**, **5k** and **5n** against *A. solani*, *S. sclerotiorum* and *P. capsici*. These results confirmed that 3-aromatic group and the *tert*-alcohol moiety played a crucial role for the antifungal activities.[33] Among these compounds, chiral lactone *R*-**5a** was broad spectrum against six fungus and the EC_{50} values were in the range of 0.2～13.5 μg/mL, which showed that it was the most active compound and could be used as the potential lead structure to improve the activity further.

After that, the typical mycelian variances of *S. sclerotiorum* treated with compounds **5a**, (*R*)-**5a**, (*S*)-**5a**, **5d**, **5j** and **5k** were observed by scanning electron microscopy (SEM) and transmission electron microscopy (TEM).[37] The SEM results showed that the mycelian variances of *S. sclerotiorum* treated by **5d** and **5j** were significant, the excessive branching mycelium was observed, and the surface of hyphae was irregular swelling (Figure **3**, B and C), while the mycelial growth which was treated by **5a**, (*R*)-**5a** and (*S*)-**5a** were strongly inhibited and the mycelial tips were not obtained for SEM observation. The TEM results indicated that the hyphal cell wall of *S. sclerotiorum* treated by (*S*)-**5a**, **5d** and **5j** became thickening irregularly, the vacuole and the internal structure were damaged, and the cell membrane was also changed (Figure 4, B, C and D). These results suggested that these compounds had a significant impact on the structure and function of the hyphal cell wall of *S. sclerotiorum* mycelium cell.[37] The further mode of action is to be made clear in the future with more experimental evidences in our laboratory.

3 Conclusion

In conclusion, the synthesis of seven-membered lactones with 3-aryl groups and *α*-hydroxyl side chains were carried out through epoxidation-lactonization procedure, and stereoselective synthesis of optical isomers of 3-aryl-7-methyl-7-hydroxy-2-octen-6-olide with Shapless asymmetric dihydroxylation as the key steps. Their structures were characterized by the IR, ^1H, ^{13}C NMR and HR-MS spectra data, and the *ee* values were analyzed by HPLC. The EC_{50} values of *R*-**5a** were in the range of 0.2～13.5 μg/mL against six phytopathgens, which showed it was the most active compound and could be used as the potential

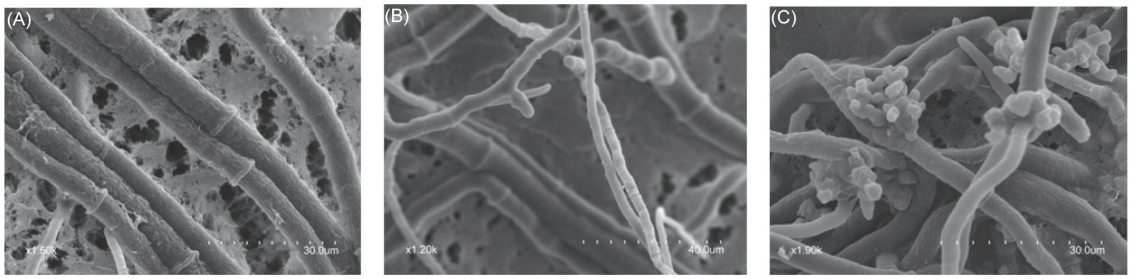


Figure 3 Mycelium growth inhibition of *S. sclerotiorum* treated with compounds **5d** and **5j** observed by SEM
(A) Blank control; (B) treated by **5d**, 50 μg/mL; (C) treated by **5j**, 50 μg/mL

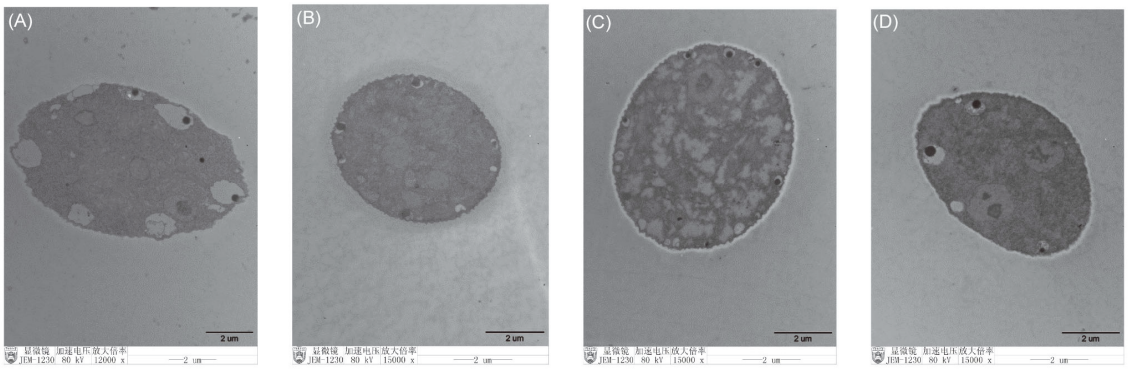


Figure 4 Cell variance of *S. sclerotiorum* treated with compounds (*S*)-**5a**, **5d** and **5j** observed by TEM
(A) Blank control; (B) treated by *S*-**5a**, 10 μg/mL; (C) treated by **5d**, 50 μg/mL; (D) treated by **5j**, 50 μg/mL

lead structure.

4 Experimental section

4.1 General information

All reactions were performed with magnetic stirring. Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. Organic solutions were concentrated under reduced pressure using a rotary evaporator or oil pump. Flash column chromatography was performed using Qingdao Haiyang silica gel (200～300 mesh). Melting points were measured on a Yanagimoto apparatus (Yanagimoto MFG Co., Kyoto, Japan) and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were obtained on Bruker DPX 300 and 400 spectrometer (Bruker Biospin Co., Stuttgart, Germany) with $CDCl_3$ as a solvent and TMS as an internal standard. HR-ESI-MS spectra were analyzed on a Bruker Apex II mass spectrometer (Bruker Co., Bremen, Germany). The solvents were analytical grade and newly distilled before usage. The *ee* values were analyzed by an Agilent LC 1100 HPLC instrument equipped with a chiral Chiralpak AD column (250 mm × 4.6 mm), eluent: hexane/isopropanol (V∶V=95∶5, 90∶10, 85∶15), flow rate: 1.0 mL/min, UV detection wavelength: 230 nm. The SEM and TEM observations were recorded on a Hitachi S-3400N scanning electron microscope and a JEOL-1230 transmission electron microscope.

4.2 Synthesis of seven-membered lactone 1-9

Compounds **1-1**～**1-7** were synthesized following the protocol, and the NMR and MS data of them were identical with that reported in the literatures.[34-35,40-42] The synthesis of (Z)-**1-3** was carried out using $NaClO_2$ as the oxidant in 88% yield, colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 11.04 (br, 1H), 6.37～6.31 (m, 1H), 5.79 (d, J=11.5 Hz, 1H), 5.13～5.12 (m, 1H), 2.71～2.66 (m, 2H), 2.18～2.13 (m, 2H), 1.70 (s, 3 H), 1.62 (s, 3H); ESI-MS *m*/*z*: 155 $[M+H]^+$.

Synthesis of seven-membered lactone **1-9** was following the procedure in the references[30-33] and purified in 83% yield, colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.50～6.43 (m, 1H), 6.01～5.97 (m, 1H), 4.07 (dd, J=8.4, 1.4 Hz, 1H), 3.12 (br, 1H), 2.55～2.51 (m, 2H), 2.25～2.18 (m, 1H), 1.92～1.88 (m, 1H), 1.30 (s, 3H), 1.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 167.82, 144.41, 121.66, 84.50, 71.43, 29.24, 27.43, 24.80, 24.55; HR-ESI-MS cacld for $C_9H_{15}O_3$ $[M+H]^+$ 171.1016, found 171.1014.

4.3 Synthesis of racemic seven-membered lactones 5

The intermediate acid (*E*)-**1-3** and (*E*)-**1-13** were prepared according to the protocol, and their spectral data were identical with that in the previous report.[36]

Took lactone **5a** as an example. To a solution of (*E*)-**1-13a** (230 mg, 1 mmol) in CH_2Cl_2 (50 mL) was added the peracetic acid solution 0.75 mL and anhydrous sodium carbonate (250 mg). The reaction mixture was stirred for 1.5 h at room temperature. After the reaction was finished as detected by thin-layer chromatography (TLC), the mixture was diluted with saturated $Na_2S_2O_3$ (50 mL) and extracted with CH_2Cl_2 (50 mL×3). The combined organic phase was washed with brine (100 mL×3), dried over anhydrous sodium sulfate, and concentrated *in vacuo* to

give a yellow liquid epoxide **1-14a**. It was directly used for the next reaction without purification. To a 100 mL three-necked flask added epoxide **1-14a** (1 mmol), 50 mL of CH_2Cl_2 and 10 mg of (+)-camphorsulfonic acid. The mixture was stirred for 4 h at room temperature. After the reaction was finished, the organic phase was washed with 5% Na_2CO_3 solution and brine, dried with anhydrous Na_2SO_4, and concentrated *in vacuo*. Flash chromatography on silica gel [petroleum ether/EtOAc (V∶V=3∶1)] afforded light yellow oil 3-phenyl-7-dimethyl-7-hydroxy-2-octen-6-olide (**5a**) 150 mg. In a similar way, compounds **5b**～**5p** were prepared.

3-Phenyl-7-dimethyl-7-hydroxy-2-octen-6-olide (**5a**): Colorless oil liquid, yield 80%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.52～7.40 (m, 5H), 6.27 (s, 1H), 4.19 (dd, J=4.5, 9.6 Hz, 1H), 2.84 (dd, J=7.5, 6.7 Hz, 2H), 2.48 (br, 1H), 2.29～2.12 (m, 2H), 1.33 (s, 6H). The ^{1}H NMR data were consistent with that reported in literature.[33]

3-(2-Chlorophenyl)-7-methyl-7-hydroxy-2-octen-6-olide (**5b**): Colorless oil liquid, yield 91%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.46～7.41 (m, 1H), 7.34～7.29 (m, 2H), 7.26～7.21 (m, 1H), 6.02 (s, 1H), 4.34 (dd, J=10.0, 3.5 Hz, 1H), 2.82 (tdd, J=9.3, 7.7, 1.9 Hz, 1H), 2.73～2.62 (m, 1H), 2.34 (s, 1H), 2.32～2.10 (m, 2H), 1.34 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.29, 153.64, 140.62, 131.26, 129.90, 129.72, 129.26, 127.09, 122.40, 84.54, 71.68, 31.61, 27.76, 25.71, 24.62; HR-MS (ESI) calcd for $C_{15}H_{18}ClO_3$ $[M+H]^+$ 281.0939, found 281.0936.

3-(3-Chlorophenyl)-7-methyl-7-hydroxy-2-octen-6-olide (**5c**): Colorless oil liquid, yield 84%. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.44～7.42 (m, 1H), 7.39～7.31 (m, 3H), 6.23 (s, 1H), 4.15 (dd, J=9.4, 4.4 Hz, 1H), 2.84～2.78 (m, 2H), 2.21～2.15 (m, 2H), 1.30 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.58, 151.75, 141.78, 134.79, 130.07, 129.42, 126.48, 124.44, 119.77, 84.13, 71.65, 30.01, 27.72, 25.73, 24.62; HR-MS (ESI) calcd for $C_{15}H_{18}ClO_3$ $[M+H]^+$ 281.0939, found 281.0933.

3-(4-Chlorophenyl)-7-methyl-7-hydroxy-2-octen-6-olide (**5d**): Colorless oil liquid, yield 69%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.44～7.34 (m, 4H), 6.23 (s, 1H), 4.16 (dd, J=9.0, 4.8 Hz, 1H), 2.86～2.78 (m, 2H), 2.45 (s, 1H), 2.25～2.13 (m, 2H), 1.31 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.79, 151.99, 138.32, 135.56, 128.99, 127.59, 119.15, 84.14, 71.64, 29.98, 27.73, 25.67, 24.64; HR-MS (ESI) calcd for $C_{15}H_{18}ClO_3$ $[M+H]^+$ 281.0939, found 281.0935.

3-(4-Methoxyphenyl)-7-methyl-7-hydroxy-2-octen-6-olide (**5e**): Colorless oil liquid, yield 61%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.45 (d, J=8.8 Hz, 2H), 6.94 (d, J=8.8 Hz, 2H), 6.21 (s, 1H), 4.16 (dd, J=9.8, 4.3 Hz, 1H), 3.86 (s, 3H), 2.84 (t, J=6.9 Hz, 2H), 2.36 (s, 1H), 2.21～2.17 (m, 2H), 1.31 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 169.07, 160.50, 152.34, 131.61, 127.39, 116.64, 113.86, 83.80, 71.36, 55.06, 29.31, 27.49, 25.52, 24.23; IR (film) v: 3438, 2971, 2927, 1684, 1596, 1508, 1223, 1161, 830, 734 cm^{-1}; HR-MS (ESI) calcd for $C_{16}H_{21}O_4$ $[M+H]^+$ 277.1434, found 277.1430.

3-(4-Methylphenyl)-7-methyl-7-hydroxy-2-octen-6-olide (**5f**): Colorless oil liquid, yield 75%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.39 (d, J=8.2 Hz, 2H), 7.23 (d, J=8.2 Hz, 2H), 6.25 (s, 1H), 4.17 (dd, J=9.6, 4.4 Hz, 1H), 2.89～2.81 (m, 2H), 2.40 (s, 3H), 2.36 (s, 1H), 2.22～2.16 (m, 2H), 1.32 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 168.90, 152.86, 139.45, 136.64, 129.17, 125.87, 117.64, 83.83, 71.35, 29.53, 27.51, 25.46, 24.29, 20.86; HR-MS (ESI) calcd for $C_{16}H_{21}O_3$ $[M+H]^+$ 261.1485, found 261.1480.

3-(4-Flurophenyl)-7-methyl-7-hydroxy-2-octen-6-olide (**5g**): Colorless oil liquid, yield 70%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.45 (dd, J=8.6, 5.3 Hz, 2H), 7.09 (t, J=8.6 Hz, 2H), 6.19 (s, 1H), 4.16 (dd, J=8.8, 5.0 Hz, 1H), 2.83 (dd, J=11.0, 4.9 Hz, 2H), 2.47 (s, 1H), 2.20～2.13 (m, 2H), 1.30 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 168.52, 163.13 (d, $^1J_{FC}$=248.6 Hz), 151.84, 135.71 (d, $^4J_{FC}$=3.4 Hz), 127.86 (d, $^3J_{FC}$=8.4 Hz), 118.46, 115.49 (d, $^2J_{FC}$=21.5 Hz), 83.83, 71.31, 29.84, 27.42, 25.34, 24.35; IR (film) v: 3441, 2979, 2930, 1684, 1602, 1511, 1248, 1179, 1029, 827, 732 cm^{-1}; HR-MS (ESI) calcd for $C_{15}H_{18}FO_3$ $[M+H]^+$ 265.1234, found 265.1229.

3-(4-Trifluromethylphenyl)-7-methyl-7-hydroxy-2-octen-6-olide (**5h**): Colorless oil liquid, yield 81%. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.66 (d, J=8.2 Hz, 2H), 7.56 (d, J=8.2 Hz, 2H), 6.27 (s, 1H), 4.17 (dd, J=9.2, 4.5 Hz, 1H), 2.88～2.80 (m, 2H), 2.25～2.16 (m, 2H), 1.31 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 167.97, 151.37, 143.28, 131.10 (q, $^2J_{FC}$=32.6 Hz), 126.36, 125.68 (q, $^3J_{FC}$=3.6 Hz), 122.76 (q, $^1J_{FC}$=274.1 Hz), 120.27, 83.82, 71.35, 29.88, 27.40, 25.38, 24.38; HR-MS (ESI) calcd for $C_{16}H_{18}F_3O_3$ $[M+H]^+$ 315.1203, found 315.1207.

3-(4-Phenylphenyl)-7-methyl-7-hydroxy-2-octen-6-olide (**5i**): Colorless oil liquid, yield 82%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.67～7.37 (m, 9H), 6.33 (s, 1H), 4.21 (dd, J=9.2, 4.8 Hz, 1H), 2.89 (dd, J=10.7, 4.4 Hz, 2H), 2.51 (s, 1H), 2.25～2.18 (m, 2H), 1.34 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 168.81, 152.42, 142.08, 139.65, 138.30, 128.60, 127.53, 127.11, 126.70, 126.45, 118.26, 83.89, 71.36, 29.52, 27.53, 25.44, 24.36; HR-MS (ESI) calcd for $C_{21}H_{23}O_3$ $[M+H]^+$ 323.1642, found 323.1640.

3-(1-Naphthyl)-7-methyl-7-hydroxy-2-octen-6-olide (**5j**): Colorless oil liquid, yield 73%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.94～7.82 (m, 3H), 7.56～7.45 (m, 3H), 7.34 (d, J=6.8 Hz, 1H), 6.17 (s, 1H), 4.41 (dd, J=7.7, 5.3 Hz, 1H), 3.08～2.93 (m, 1H), 2.81～2.70 (m, 1H), 2.31～2.19 (m, 2H), 1.39 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.37, 155.24, 139.65, 133.69, 129.87, 128.83, 128.66, 126.69, 126.23, 125.15, 124.80, 124.66, 122.19, 84.52, 71.79, 33.71, 27.98, 25.51, 24.74; HR-MS (ESI) calcd for $C_{19}H_{21}O_3$ $[M+H]^+$ 297.1485, found 297.1489.

3-(2-Naphthyl)-7-methyl-7-hydroxy-2-octen-6-olide (**5k**): Colorless oil liquid, yield 84%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.95 (s, 1H), 7.89～7.84 (m, 3H), 7.60～7.52 (m, 3H), 6.40 (s, 1H), 4.24 (dd, J=9.2, 4.8 Hz, 1H), 2.99～2.90 (m, 2H), 2.43 (s, 1H), 2.31～2.20 (m, 2H), 1.34 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 168.91,

152.82, 136.71, 133.28, 132.73, 128.30, 128.14, 127.33, 126.75 126.49, 125.66, 123.36, 118.78, 83.93, 71.38, 29.59, 27.59, 25.46, 24.34; HR-MS (ESI) calcd for $C_{19}H_{21}O_3$ $[M+H]^+$ 297.1485, found 297.1482.

3-(4-Acetylphenyl)-7-methyl-7-hydroxy-2-octen-6-olide (**5l**): Colorless oil liquid, yield 68%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.00 (d, J=8.5 Hz, 2H), 7.56 (d, J=8.5 Hz, 2H), 6.31 (s, 1H), 4.19 (dd, J=9.2, 4.6 Hz, 1H), 2.87 (t, J=6.7 Hz, 2H), 2.64 (s, 3H), 2.36～2.17 (m, 3H), 1.33 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 196.88, 168.06, 151.55, 144.12, 137.24, 128.45, 126.22, 120.13, 83.79, 71.35, 29.68, 27.41, 26.31, 25.44, 24.38; HR-MS (ESI) calcd for $C_{17}H_{21}O_4$ $[M+H]^+$ 289.1434, found 289.1437.

3-(4-Ethoxycarbonylphenyl)-7-methyl-7-hydroxy-2-octen-6-olide (**5m**): Colorless oil liquid, yield 78%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.07 (d, J=8.4 Hz, 2H), 7.53 (d, J=8.4 Hz, 2H), 6.30 (s, 1H), 4.19 (dd, J=8.9, 4.9 Hz, 1H), 3.94 (s, 3H), 2.86 (t, J=6.9 Hz, 2H), 2.30～2.16 (m, 2H), 1.32 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 168.29, 166.06, 151.84, 144.03, 130.56, 129.70, 125.99, 120.00, 83.87, 71.35, 51.97, 29.71, 27.44, 25.36, 24.34; HR-MS (ESI) calcd for $C_{17}H_{21}O_5$ $[M+H]^+$ 305.1384, found 305.1380.

3-(4-*t*-Butylphenyl)-7-methyl-7-hydroxy-2-octen-6-olide (**5n**): Colorless oil liquid, yield 90%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.44 (brs, 4H), 6.27 (s, 1H), 4.17 (dd, J=9.8, 4.3 Hz, 1H), 2.90～2.81 (m, 2H), 2.26～2.14 (m, 2H), 1.35 (s, 9H), 1.31 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 169.01, 152.71, 136.46, 125.73, 125.44, 117.65, 83.88, 71.36, 34.40, 30.84, 29.36, 27.53, 25.50, 24.22; HR-MS (ESI) calcd for $C_{19}H_{27}O_3$ $[M+H]^+$ 303.1955, found 303.1961.

3-(4-Cyanophenyl)-7-methyl-7-hydroxy-2-octen-6-olide (**5o**): Colorless oil liquid, yield 65%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.72 (d, J=8.6 Hz, 2H), 7.57 (d, J=8.6 Hz, 2H), 6.29 (s, 1H), 4.17 (dd, J=9.2, 4.5 Hz, 1H), 2.88～2.80 (m, 2H), 2.25～2.17 (m, 2H), 1.32 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 167.70, 150.68, 144.16, 132.27, 126.68, 120.94, 117.82, 112.74, 83.78, 71.33, 29.67, 27.34, 25.36, 24.44; HR-MS (ESI) calcd for $C_{16}H_{18}NO_3$ $[M+H]^+$ 272.1281, found 272.1283.

3-(2-Methoxyphenyl)-7-methyl-7-hydroxy-2-octen-6-olide (**5p**): Colorless oil liquid, yield 88%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.35 (dd, J=8.2, 1.7 Hz, 1H), 7.20 (dd, J=7.5, 1.7 Hz, 1H), 7.00～6.90 (m, 2H), 6.04 (s, 1H), 4.28 (dd, J=10.0, 4.9 Hz, 1H), 3.85 (s, 3H), 2.76～2.66 (m, 2H), 2.24～2.13 (m, 2H), 1.33 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 169.34, 155.97, 153.89, 130.33, 129.88, 128.62, 120.49, 120.46, 110.60, 84.36, 71.40, 55.11, 30.16, 27.39, 25.61, 24.19; HR-MS (ESI) calcd for $C_{16}H_{21}O_4$ $[M+H]^+$ 277.1434, found 277.1436.

3-(2-Methylphenyl)-7-methyl-7-hydroxy-2-octen-6-olide (**5q**): Colorless oil liquid, yield 81%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.29～7.17 (m, 3H), 7.11 (d, J=7.0 Hz, 1H), 5.94 (s, 1H), 4.26 (dd, J=9.0, 3.8 Hz, 1H), 2.87～2.74 (m, 1H), 2.63～2.49 (m, 2H), 2.33 (s, 3H), 2.22～2.11 (m, 2H), 1.34 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 168.03, 155.98, 141.36, 133.50, 130.29, 127.97, 126.90, 125.62, 120.90, 84.17, 71.38, 32.81, 27.45, 25.14, 24.41, 19.57; IR (film) ν: 3432, 2971, 2924, 1684, 1271, 1230, 1062, 758, 726 cm^{-1}; HR-MS (ESI) calcd for $C_{16}H_{21}O_3$ $[M+H]^+$ 261.1485, found 261.1487.

3-(2,4-Dimethylphenyl)-7-methyl-7-hydroxy-2-octen-6-olide (**5r**): Colorless oil liquid, yield 79%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.06～7.00 (m, 3H), 5.93 (s, 1H), 4.25 (dd, J=8.8, 4.2 Hz, 1H), 2.87～2.72 (m, 2H), 2.58～2.40 (m, 1H), 2.34 (s, 3H), 2.30 (s, 3H), 2.22～2.12 (m, 2H), 1.34 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 168.17, 156.01, 138.54, 137.83, 133.41, 131.06, 126.93, 126.27, 120.78, 84.13, 71.39, 32.80, 27.45, 25.16, 24.40, 20.69, 19.57; HR-MS (ESI) calcd for $C_{17}H_{23}O_3$ $[M+H]^+$ 275.1642, found 275.1648.

3-(3,5-Dimethylphenyl)-7-methyl-7-hydroxy-2-octen-6-olide (**5s**): Colorless oil liquid, yield 85%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.08 (d, J=2.4 Hz, 2H), 7.05 (t, J=2.4 Hz, 1H), 6.23 (s, 1H), 4.17 (dd, J=9.2, 4.8 Hz, 1H), 2.87～2.79 (m, 2H), 2.50 (s, 1H), 2.36 (s, 6H), 2.24～2.15 (m, 2H), 1.32 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 169.08, 153.59, 139.71, 138.02, 130.80, 123.84, 118.05, 83.94, 71.35, 29.80, 27.57, 25.33, 24.34, 20.96; HR-MS (ESI) calcd for $C_{17}H_{23}O_3$ $[M+H]^+$ 275.1642, found 275.1646.

4.4 Synthesis of *R*-**5a**～*S*-**5n** via Sharpless asymmetric dihydroxylation

4.4.1 Synthesis of **15a**～**15d**

To a 250 mL flask, (*E*)-**1-13a** (660 mg, 2.87 mmol), methanol (0.5 mL), *N*,*N*-dicyclohexylcarbodiimide (675 mg, 3.28 mmol), 4-*N*,*N*-dimethylaminopyridine (34 mg, 0.31 mmol) and dry CH_2Cl_2 (100 mL) were added, the mixture was stirred at room temperature under argon atmosphere for 5 h. A white solid was filtered off. The organic solution was washed with water and dried over anhydrous Na_2SO_4, removed the solid and concentrated under vacuum. Then the crude material was purified by column chromatography on silica gel [petroleum ether/EtOAc (V∶V=100∶1)] to afford colorless oil **15a** 560 mg, yield 80%. In a similar way, the esters **15b**～**15d** was prepared.

Methyl (2*E*)-3-phenyl-7-methylocta-2,6-dienoate (**15a**): ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.45 (dt, J=5.2, 2.2 Hz, 2H), 7.39 (dd, J=7.6, 3.0 Hz, 3H), 6.06 (s, 1H), 5.16 (t, J=7.2 Hz, 1H), 3.77 (s, 3H), 3.23～3.07 (m, 2H), 2.13 (t, J=7.5 Hz, 2H), 1.67 (s, 3H), 1.54 (s, 3H); HR-MS (ESI) calcd for $C_{16}H_{21}O_2$ $[M+H]^+$ 245.1536, found 245.1541.

Methyl (2*E*)-3-(4-phenylphenyl)-7-methylocta-2,6-dienoate (**15b**): ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.41 (brs, 4H), 6.08 (s, 1H), 5.16 (t, J=7.1 Hz, 1H), 3.76 (s, 3H), 3.17～3.07 (m, 2H), 2.14 (t, J=7.6 Hz, 2H), 1.67 (s, 3H), 1.56 (s, 3H), 1.35 (s, 9H); HR-MS (ESI) calcd for $C_{22}H_{25}O_2$ $[M+H]^+$ 321.1849, found 321.1848.

Methyl (2*E*)-3-(4-*tert*-butylphenyl)-7-methylocta-2,6-dienoate (**15c**): ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.63 (brs, 4H), 7.57～7.52 (m, 2H), 7.47 (t, J=7.2 Hz, 2H), 7.38 (t, J=7.2 Hz, 1H), 6.13 (s, 1H), 5.19 (t, J=7.2 Hz, 1H), 3.78

(s, 3H), 3.23～3.14 (m, 2H), 2.18 (t, J=7.5 Hz, 2H), 1.68 (s, 3H), 1.56 (s, 3H); HR-MS (ESI) calcd for $C_{20}H_{29}O_2$ $[M+H]^+$ 301.2168, found 301.2164.

Methyl (2*E*)-3-(2-naphthyl)-7-methylocta-2,6-dienoate (**15d**): ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.01～7.79 (m, 4H), 7.63～7.48 (m, 3H), 6.21 (s, 1H), 5.20 (d, J=7.2 Hz, 1H), 3.80 (s, 3H), 3.35～3.19 (m, 2H), 2.19 (t, J=7.2 Hz, 2H), 1.68 (s, 3H), 1.54 (s, 3H); HR-MS (ESI) calcd for $C_{20}H_{23}O_2$ $[M+H]^+$ 295.1693, found 295.1686.

4.4.2 Synthesis of **16**～**19**

A 100 mL round-bottomed flask equipped with a magnetic stirring bar was charged with AD-mix-β (3.9 g), water (20 mL) and *tert*-butyl alcohol (20 mL). The resulting mixture was stirred at room temperature to produce two clear phases. Methanesulfonamide (185 mg, 1.95 mmol) was added in one-portion and the reaction mixture was stirred for 1.5 h. The reaction mixture was cooled to 0 ℃. Compound **15a** (430 mg, 3.0 mmol) was added at once, and the heterogeneous slurry was stirred vigorously at 0 ℃ for 40 h. The saturated $Na_2S_2O_3$ solution (40 mL) was added at 0 ℃, and the mixture was allowed to room temperature and stirred for 30 min. EtOAc (50 mL) and water (50 mL) were added to the reaction mixture. The organic layer was separated and the aqueous layer was re-extracted with EtOAc (50 mL×3). The combined organic phase was dried over with anhydrous Na_2SO_4, and the solvent was removed to give the crude product. This product was purified by flash chromatography on silica gel with petroleum ether/EtOAc (V∶V=3∶1) as the eluent to give colorless oil methyl (2*E*,6*R*)-3-phenyl-7-methyl-6,7-dihydroxy-octa-2-enoate (**16a**) 382 mg, yield 78%. In a similar way, the chiral diol esters **16**～**19** was prepared.

Methyl (2*E*,6*R*)-3-phenyl-7-methyl-6,7-dihydroxy-octa-2-enoate (**16a**): Colorless liquid, yield 78%, 98.4% *ee*. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.46～7.36 (m, 5H), 6.12 (s, 1H), 3.80 (s, 3H), 3.51 (dt, J=13.2, 8.3 Hz, 1H), 3.38～3.29 (m, 1H), 3.02～2.89 (m, 1H), 1.54 (t, J=7.5 Hz, 2H), 1.07 (s, 3H), 1.04 (s, 3H); HR-MS (ESI) calcd for $C_{16}H_{23}O_4$ $[M+H]^+$ 279.1591, found 279.1595.

Methyl (2*E*,6*S*)-3-phenyl-7-methyl-6,7-dihydroxy-octa-2-enoate (**16b**): Colorless liquid, yield 86%, 94.3% *ee*. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.45～7.35 (m, 5H), 6.12 (s, 1H), 4.07 (s, 1H), 3.79 (s, 3H), 3.52 (dt, J=13.2, 8.1 Hz, 1H), 3.39～3.30 (m, 1H), 3.01～2.88 (m, 1H), 2.67 (s, 1H), 1.54 (t, J=7.5 Hz, 2H), 1.08 (s, 3H), 1.04 (s, 3H); HR-MS (ESI) calcd for $C_{16}H_{23}O_4$ $[M+H]^+$ 279.1591, found 279.1589.

Methyl (2*E*,6*R*)-3-(4-phenylphenyl)-7-methyl-6,7-dihydroxy-octa-2-enoate (**17a**): Colorless liquid, yield 54%, 98.7% *ee*. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.43～7.36 (m, 4H), 6.14 (s, 1H), 4.10 (s, 1H), 3.77 (s, 3H), 3.55～3.42 (m, 1H), 3.35 (d, J=9.4 Hz, 1H), 3.03～2.92 (m, 1H), 1.63～1.51 (m, 2H), 1.34 (s, 9H), 1.09 (s, 3H), 1.06 (s, 3H); HR-MS (ESI) calcd for $C_{22}H_{27}O_4$ $[M+H]^+$ 355.1904, found 355.1900.

Methyl (2*E*,6*S*)-3-(4-phenylphenyl)-7-methyl-6,7-dihydroxy-octa-2-enoate (**17b**): Colorless liquid, yield 83%, 95.9% *ee*. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.43～7.36 (m, 4H), 6.14 (s, 1H), 4.05 (s, 1H), 3.77 (s, 3H), 3.54～3.42 (m, 1H), 3.35 (d, J=9.5 Hz, 1H), 3.04～2.93 (m, 1H), 2.65 (s, 1H), 1.63～1.52 (m, 2H), 1.34 (s, 9H), 1.09 (s, 3H), 1.06 (s, 3H); HR-MS (ESI) calcd for $C_{22}H_{27}O_4$ $[M+H]^+$ 355.1901, found 355.1902.

Methyl (2*E*,6*R*)-3-(4-*tert*-butylphenyl)-7-methyl-6,7-dihydroxy-octa-2-enoate (**18a**): Colorless liquid, yield 80% 98.9% *ee*. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.68～7.63 (m, 4H), 7.56～7.44 (m, 4H), 7.39 (t, J=7.2 Hz, 1H), 6.20 (s, 1H), 4.07 (s, 1H), 3.80 (s, 3H), 3.54～3.43 (m, 1H), 3.39 (d, J=8.4 Hz, 1H), 3.08～2.97 (m, 1H), 2.68 (s, 1H), 1.67～1.53 (m, 2H), 1.11 (s, 3H), 1.08 (s, 3H); HR-MS (ESI) calcd for $C_{20}H_{31}O_4$ $[M+H]^+$ 335.2217, found 335.2214.

Methyl (2*E*,6*S*)-3-(4-*tert*-butylphenyl)-7-methyl-6,7-dihydroxy-octa-2-enoate (**18b**): Colorless liquid, yield 81%, 94.8% *ee*. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.67～7.62 (m, 4H), 7.56～7.44 (m, 4H), 7.39 (t, J=7.2 Hz, 1H), 6.20 (s, 1H), 4.10 (s, 1H), 3.80 (s, 3H), 3.55～3.43 (m, 1H), 3.39 (d, J=8.4 Hz, 1H), 3.09～2.95 (m, 1H), 2.68 (s, 1H), 1.67～1.54 (m, 2H), 1.10 (s, 3H), 1.08 (s, 3H); HR-MS (ESI) calcd for $C_{20}H_{31}O_4$ $[M+H]^+$ 335.2217, found 335.2218.

Methyl (2*E*,6*R*)-3-(2-naphthyl)-7-methyl-6,7-dihydroxy-octa-2-enoate (**19a**): Colorless liquid, yield 80%, 98.7% *ee*. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.95～7.83 (m, 4H), 7.58～7.50 (m, 3H), 6.27 (s, 1H), 4.09 (d, J=3.5 Hz, 1H), 3.81 (s, 3H), 3.66～3.55 (m, 1H), 3.41 (s, 1H), 3.16～3.02 (m, 1H), 2.62 (s, 1H), 1.67～1.53 (m, 3H), 1.07 (s, 3H), 1.02 (s, 3H); HR-MS (ESI) calcd for $C_{20}H_{25}O_4$ $[M+H]^+$ 329.1747, found 329.1743.

Methyl (2*E*,6*S*)-3-(2-naphthyl)-7-methyl-6,7-dihydroxy-octa-2-enoate (**19b**): Colorless liquid, yield 73%, 95.6% *ee*. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.95～7.83 (m, 4H), 7.58～7.50 (m, 3H), 6.27 (s, 1H), 4.10 (d, J=3.5 Hz, 1H), 3.81 (s, 3H), 3.66～3.55 (m, 1H), 3.41 (s, 1H), 3.16～3.05 (m, 1H), 2.64 (s, 1H), 1.65～1.53 (m, 3H), 1.07 (s, 3H), 1.02 (s, 3H); HR-MS (ESI) calcd for $C_{20}H_{25}O_4$ $[M+H]^+$ 329.1747, found 329.1749.

4.4.3 Synthesis of **20**～**23**

(2*E*,6*R*)-3-Phenyl-7-methyl-6,7-dihydroxy-octa-2-enoic acid (**20a**): To a solution of compound **16a** (410 mg, 1.47 mmol) in 50 mL CH_3OH/H_2O (V∶V=1∶1) was added LiOH•H_2O (100 mg, 2.4 mmol). After being stirred for 5 h at 40 ℃, the reaction mixture was diluted with water and washed with ether. The aqueous layer was acidified with concentrated hydrochloric acid to pH=2 and extracted with ethyl acetate (50 mL×3). The organic extract was combined, dried over anhydrous Na_2SO_4, filtered, and concentrated to give the crude product, which was purified by flash chromatography on silica gel with petroleum ether/EtOAc (V∶V=3∶1) as the eluent to give Colorless oil chiral diol acid **20a** 277 mg, yield 71%. In a similar way, the chiral diol acids **20b**～**23b** was prepared.

(2*E*,6*R*)-3-Phenyl-7-methyl-6,7-dihydroxy-octa-2-enoic acid (**20a**): Colorless liquid, yield 71%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.50～7.40 (m, 5H), 6.16 (s, 1H), 5.31 (s, 2H), 3.52 (dt, J=13.3, 8.4 Hz, 1H), 3.41 (dd, J=8.5, 4.1 Hz, 1H), 3.07～2.96 (m, 1H), 1.56 (t, J=7.6 Hz, 2H), 1.10 (s, 3H), 1.07 (s, 3H); HR-MS (ESI) calcd for $C_{15}H_{21}O_4$ $[M+H]^+$ 265.1434, found 265.1438.

(2*E*,6*S*)-3-Phenyl-7-methyl-6,7-dihydroxy-octa-2-enoic acid (**20b**): Colorless liquid, yield 84%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.50～7.41 (m, 5H), 6.16 (s, 1H), 5.52 (s, 2H), 3.52 (dt, J=13.3, 8.4 Hz, 1H), 3.41 (dd, J=8.5, 4.0 Hz, 1H), 3.06～2.96 (m, 1H), 1.56 (t, J=7.6 Hz, 2H), 1.10 (s, 3H), 1.07 (s, 3H); HR-MS (ESI) calcd for $C_{15}H_{21}O_4$ $[M+H]^+$ 265.1434, found 265.1435.

(2*E*,6*R*)-3-(Phenylphenyl)-7-methyl-6,7-dihydroxy-octa-2-enoic acid (**21a**): Colorless liquid, yield 78%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.39 (brs, 4H), 6.15 (s, 1H), 3.50～3.40 (m, 1H), 3.10～2.96 (m, 1H), 1.57 (d, J=5.5 Hz, 2H), 1.32 (s, 9H), 1.09 (s, 3H), 1.08 (s, 3H); HR-MS (ESI) calcd for $C_{21}H_{25}O_4$ $[M+H]^+$ 341.1747, found 341.1745.

(2*E*,6*S*)-3-(Phenylphenyl)-7-methyl-6,7-dihydroxy-octa-2-enoic acid (**21b**): Colorless liquid, yield 74%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.39 (brs, 4H), 6.15 (s, 1H), 3.51～3.37 (m, 1H), 3.10～2.98 (m, 1H), 1.57 (d, J=5.9 Hz, 2H), 1.32 (s, 9H), 1.09 (s, 3H), 1.08 (s, 3H); HR-MS (ESI) calcd for $C_{21}H_{25}O_4$ $[M+H]^+$ 341.1747, found 341.1752.

(2*E*,6*R*)-3-(4-*tert*-Butylphenyl)-7-methyl-6,7-dihydroxy-octa-2-enoic acid (**22a**): Colorless liquid, yield 67%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.63～7.57 (m, 4H), 7.52 (d, J=7.3 Hz, 2H), 7.44 (t, J=7.3 Hz, 2H), 7.36 (t, J=7.2 Hz, 1H), 6.23 (s, 1H), 3.50～3.47 (m, 2H), 3.09 (s, 1H), 1.60 (t, J=6.6 Hz, 2H), 1.11 (s, 3H), 1.10 (s, 3H); HR-MS (ESI) calcd for $C_{19}H_{29}O_4$ $[M+H]^+$ 321.2060, found 321.2056.

(2*E*,6*S*)-3-(4-*tert*-Butylphenyl)-7-methyl-6,7-dihydroxy-octa-2-enoic acid (**22b**): Colorless liquid, yield 78%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.62～7.57 (m, 4H), 7.54 (d, J=7.2 Hz, 2H), 7.46 (t, J=7.2 Hz, 2H), 7.39 (d, J=7.2 Hz, 1H), 6.24 (s, 1H), 3.51～3.48 (m, 2H), 3.09 (s, 1H), 1.61 (t, J=6.5 Hz, 2H), 1.12 (s, 3H), 1.11 (s, 3H); HR-MS (ESI) calcd for $C_{19}H_{29}O_4$ $[M+H]^+$ 321.2060, found 321.2064.

(2*E*,6*R*)-3-(2-Naphthyl)-7-methyl-6,7-dihydroxy-octa-2-enoic acid (**23a**): Colorless liquid, yield 86%. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 12.20 (s, 1H), 8.08 (s, 1H), 7.98～7.90 (m, 3H), 7.65 (dd, J=8.6, 1.8 Hz, 1H), 7.57～7.50 (m, 2H), 6.14 (s, 1H), 4.03 (s, 1H), 3.23～3.11 (m, 2H), 1.72～1.55 (m, 1H), 1.31～1.17 (m, 1H), 0.97 (s, 3H), 0.88 (s, 3H); HR-MS (ESI) calcd for $C_{19}H_{23}O_4$ $[M+H]^+$ 315.1591, found 315.1594.

(2*E*,6*S*)-3-(2-Naphthyl)-7-methyl-6,7-dihydroxy-octa-2-enoic acid (**23b**): Colorless liquid, yield 83%. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.08 (s, 1H), 8.00～7.89 (m, 3H), 7.65 (dd, J=8.6, 1.8 Hz, 1H), 7.56～7.50 (m, 2H), 6.14 (s, 1H), 4.02 (s, 1H), 3.22～3.10 (m, 2H), 1.72～1.55 (m, 2H), 1.30～1.17 (m, 1H), 0.97 (s, 3H), 0.88 (s, 3H); HR-MS (ESI) calcd for $C_{19}H_{23}O_4$ $[M+H]^+$ 315.1591, found 315.1589.

4.4.4 Synthesis of *R*-**5a** ~ *S*-**5n**

To a stirred solution of chiral hydroxyl acid **20a** (173 mg, 0.66 mmol) in tetrahydrofuran (THF) 10 mL was added Et_3N (0.20 mL, 1.4 mmol) at 0 ℃, and 2,4,6-trichlorobenzoyl chloride (0.3 mL, 1.92 mmol). After reaction 1 h, the mixture was diluted with THF (10 mL) and a solution of 4-*N*,*N*-dimethylaminopyridine (DMAP) (0.47 g, 3.9 mmol) in 100 mL toluene was added slowly at room temperature. The solution was heated to 100 ℃ for 12 h, and allowed to cool to room temperature. The solution was washed with saturated aqueous NaCl and extracted with EtOAc (100 mL×3). The organic phase was dried over anhydrous Na_2SO_4, the solvent was removed in vacuo, and the residue was purified by chromatography on silica gel, eluted with petroleum ether/EtOAc (V∶V=3∶1) to give (*R*)-3-phenyl-7-methyl-6,7-dihydroxy-2-octen-6-olide (*R*-**5a**) as colorless oil 130 mg. In similar way, compounds *S*-**5a**, *R*-**5i** and *S*-**5i**, *R*-**5k** and *S*-**5k**, *R*-**5n** and *S*-**5n** were prepared replacing **20a** with **20b**, **21a**, **21b**, **22a**, **22b**, **23a** and **23b**, respectively.

(*R*)-3-Phenyl-7-methyl-6,7-dihydroxy-2-octen-6-olide (*R*-**5a**): Colorless oil, yield 81%, *ee* 96.5%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.48～7.37 (m, 5H), 6.24 (s, 1H), 4.17 (dd, J=9.6, 4.5 Hz, 1H), 2.84 (dd, J=7.5, 6.7 Hz, 2H), 2.42 (s, 1H), 2.26～2.12 (m, 2H), 1.30 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 168.71, 152.96, 139.66, 129.16, 128.47, 125.95, 118.50, 83.85, 71.35, 29.70, 27.50, 25.42, 24.34; HR-MS (ESI) calcd for $C_{15}H_{19}O_3$ $[M+H]^+$ 247.1329, found 247.1325.

(*S*)-3-Phenyl-7-methyl-6,7-dihydroxy-2-octen-6-olide (*S*-**5a**): Colorless oil, yield 75%, *ee* 94.1%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.48～7.37 (m, 5H), 6.24 (s, 1H), 4.17 (dd, J=9.6, 4.5 Hz, 1H), 2.84 (dd, J=7.5, 6.7 Hz, 2H), 2.41 (s, 1H), 2.24～2.12 (m, 2H), 1.30 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 168.71, 152.96, 139.67, 129.17, 128.48, 125.96, 118.50, 83.85, 71.35, 29.71, 27.50, 25.44, 24.35; HR-MS (ESI) calcd for $C_{15}H_{19}O_3$ $[M+H]^+$ 247.1329, found 247.1327.

(*R*)-3-(4-Phenylphenyl)-7-methyl-6,7-dihydroxy-2-octen-6-olide (*R*-**5i**): Colorless oil, yield 66%, *ee* 98.0%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.66～7.35 (m, 9H), 6.32 (s, 1H), 4.19 (dd, J=9.5, 4.5 Hz, 1H), 2.91～2.85 (m, 2H), 2.56 (s, 1H), 2.25～2.15 (m, 2H), 1.32 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 168.83, 152.42, 142.10, 139.66, 138.28, 128.59, 127.53, 127.12, 126.70, 126.45, 118.24, 83.88, 71.41, 29.49, 27.52, 25.50, 24.29; IR (film) ν: 3441, 2973, 2919, 1684, 1275, 1229, 1065, 833, 766, 697 cm^{-1}; HR-MS (ESI) calcd for $C_{21}H_{23}O_3$ $[M+H]^+$ 323.1642, found 323.1638.

(*S*)-3-(4-Phenylphenyl)-7-methyl-6,7-dihydroxy-2-octen-6-olide (*S*-**5i**): Colorless oil, yield 67%, *ee* 94.1%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.66～7.35 (m, 9H), 6.31 (s, 1H), 4.19 (dd, J=9.5, 4.5 Hz, 1H), 2.90～2.85 (m, 2H), 2.73 (s, 1H), 2.24～2.16 (m, 2H), 1.32 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 168.84, 152.48, 142.06, 139.64,

138.32, 128.60, 127.53, 127.10, 126.70, 126.46, 118.25, 83.90, 71.37, 29.56, 27.52, 25.38, 24.42; HR-MS (ESI) calcd for $C_{21}H_{23}O_3$ $[M+H]^+$ 323.1642, found 323.1637.

(*R*)-3-(4-*tert*-Butylphenyl)-7-methyl-6,7-dihydroxy-2-octen-6-olide (*R*-**5k**): Colorless oil, yield 69%, *ee* 97.8%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.95 (s, 1H), 7.89～7.84 (m, 3H), 7.60～7.52 (m, 3H), 6.39 (s, 1H), 4.24 (dd, J= 9.5, 4.6 Hz, 1H), 2.99～2.90 (m, 2H), 2.41 (s, 1H), 2.30～2.19 (m, 2H), 1.33 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 168.91, 152.82, 136.71, 133.28, 132.73, 128.30, 128.14, 127.33, 126.75 126.49, 125.66, 123.36, 118.78, 83.93, 71.38, 29.59, 27.59, 25.46, 24.34; HR-MS (ESI) calcd for $C_{19}H_{21}O_3$ $[M+H]^+$ 297.1485, found 297.1480.

(*S*)-3-(4-*tert*-Butylphenyl)-7-methyl-6,7-dihydroxy-2-octen-6-olide (S-**5k**): Colorless oil, yield 72%, *ee* 94.8%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.95 (s, 1H), 7.89～7.84 (m, 3H), 7.61～7.52 (m, 3H), 6.40 (s, 1H), 4.24 (dd, J= 9.5, 4.8 Hz, 1H), 2.98～2.90 (m, 2H), 2.43 (s, 1H), 2.31～2.20 (m, 2H), 1.34 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 168.90, 152.82, 136.72, 133.27, 132.73, 128.29, 128.14, 127.35, 126.75 126.50, 125.64, 123.37, 118.78, 83.92, 71.40, 29.59, 27.60, 25.48, 24.35; HR-MS (ESI) calcd for $C_{19}H_{21}O_3$ $[M+H]^+$ 297.1485, found 297.1482.

(*R*)-3-(2-Naphthyl)-7-methyl-6,7-dihydroxy-2-octen-6-olide (*R*-**5n**): Colorless oil, yield 86%, *ee* 95.0%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.42 (s, 4H), 6.25 (s, 1H), 4.15 (dd, J=9.8, 4.3 Hz, 1H), 2.83 (dd, J=11.1, 5.4 Hz, 2H), 2.24～2.12 (m, 2H), 1.33 (s, 9H), 1.30 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 168.99, 152.71, 152.68, 136.49, 125.73, 125.43, 117.66, 83.87, 71.33, 34.39, 30.85, 29.40, 27.51, 25.42, 24.33; HR-MS (ESI) calcd for $C_{19}H_{27}O_3$ $[M+H]^+$ 303.1955, found 303.1951.

(*S*)-3-(2-Naphthyl)-7-methyl-6,7-dihydroxy-2-octen-6-olide (*S*-**5n**): Colorless oil, yield 91%, *ee* 97.7%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.42 (s, 4H), 6.25 (s, 1H), 4.15 (dd, J=9.8, 4.3 Hz, 1H), 2.83 (dd, J=11.1, 5.4 Hz, 2H), 2.24～2.12 (m, 2H), 1.33 (s, 9H), 1.30 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 168.96, 152.70, 152.66, 136.47, 125.73, 125.44, 117.66, 83.85, 71.35, 34.40, 30.85, 29.36, 27.52, 25.50, 24.25; HR-MS (ESI) calcd for $C_{19}H_{27}O_3$ $[M+H]^+$ 303.1955, found 303.1950.

4.5 Bioassay of fungicidal activity

The fungicidal activities of compounds **5a**～**5s** against *R. Solani*, *A. Solani*, *F. graminearum*, *S. Sclerotiorum*, *B. cinerea* and *P. capsici* were evaluated using methods in the references[33,37-39] by the mycelium growth rate.

Procedure for inhibition rate: The stock 2000 mg/L dimethyl sulfoxide (DMSO) solution of tested compounds were prepared in advance. Then hot potato dextrose agar (PDA) culture medium was added into a plate, the sample solution or blank DMSO was added to the plate and mixed with PDA culture medium to make the final concentration as desired. When plate was made, a 5 mm diameter fungus cake was put into the center of plate. The plate was incubated at 25 ± 0.5 °C for 24～48 h, checked the growth status and calculated the inhibition rate according to the reference. Three replicates were performed and the mean measurements were calculated from the three replicates for each concentration. The EC_{50} values were determined from the inhibition rates of five different concentrations based on the statistics method for the compounds which had more than 70% inhibition rates in the preliminary evaluation. Carbendazim and chlorothalonil were used as the positive control in the mycelium growth rate test.

4.6 Scanning electron microscopy (SEM) and transmission electron microscopy (TEM)

The samples were treated for scanning electron microscopy and transmission electron microscopy as in the previous paper.[37]

Scanning electron microscopy: *S. Sclerotiorum* mycelial tips (5 mm) of an actively growing colony on PDA medium amended with 0, 10, 50, and 100 μg/mL of compounds **5d**, **5j** and **5k** were cut from the edge of the colony cultured for 48 h. The tips were treated with 2% glutaraldehyde at 4 ℃, followed by rinsing with 0.1 mol/L phosphate buffer (pH 7.3) and fixed with 1% (mass fraction) osmium tetraoxide solution. Rinsed with 0.1 mol/L phosphate buffer three times, the mycelial tips were dehydrated using a series of ethanol solutions in the order of concentrations 30%, 50%, 70%, 80%, 90% and 100%. The processes of drying at critical point, mounting, and gold spraying were completed at last and examined with a Hitachi S-3400N scanning electron microscope with an accelerating voltage of 18～20 kV.

Transmission electron microscopy: The mycelial tips which treated by (*S*)-**5a**, **5d** and **5j** were prepared according to the method given above. After dehydrating with acetone and embedding in SPURR resin, thin sections were cut with LEICAUCi machine, and double-stained with uranyl acetate and lead citrate. The grids were examined with a JEOL-1230 transmission electron microscope.

Supporting Information The ^{1}H NMR, ^{13}C NMR and HR-ESI-MS spectra of compounds **5a**～**5s** and *R*-**5a**～*S*-**5n**, HPLC profiles of **5a**, **5n** and intermediates **16**～**19**. The Supporting Information is available free of charge via the Internet at http://sioc-journal.cn.

References

[1] Gabriela, L.; Gallardo, N. I. P.; Cabrera, G. M. *Phytochem. Lett.* **2008**, *1*, 155.

[2] Yang, Y.; Jiang, J. Z.; Qimei, L. B.; Yan, X. J.; Zhao, J. X.; Yuan, H. Z.; Qin, Z. H.; Wang, M. A. *Molecules* **2010**, *15*, 7075.

[3] Schulz, S.; Hotling, S. *Nat. Prod. Rep.* **2015**, *32*, 1042.

[4] Davies-Coleman, M. T.; Rivett, D. E. A. *Prog. Chem. Org. Nat. Prod.* **1989**, *55*, 1.

[5] Collett, L. A.; Davies-Coleman, M. T.; Rivett, D. E. A. *Prog. Chem. Org. Nat. Prod.* **1998**, *75*, 182.

[6] Pereda-Miranda, R.; Fragoso-Serrano, M.; Cerda-Garcia-Rojas, C. M. *Tetrahedron* **2001**, *57*, 47.

[7] Hoffmann, H. M. R.; Rabe, J. *Angew. Chem., Int. Ed.* **1985**, *24*, 94.

[8] Marco, J. A.; Carda, M.; Murga, J.; Falomir, E. *Tetrahedron* **2007**, *63*, 2929.

[9] Boucard, V.; Broustal, G.; Campagne, J. M. *Eur. J. Org. Chem.*

2007, 225.
[10] Gerard, R. *Tetrahedron* **1995**, *51*, 2777.
[11] Helena, M. C.; Fernanda, I. B.; Myrian, K. S.; Luiz, S. L. J. *Quim. Nova* **2008**, *31*, 885.
[12] Helena, M. C.; Fernanda, I. B.; Luiz, S. L. J. *Synthesis* **2007**, 3261.
[13] Shiina, I. *Chem. Rev.* **2007**, *107*, 239.
[14] Chang, H.-T.; Jayanth, T. T.; Wang, C.-C.; Cheng, C.-H. *J. Am. Chem. Soc*. **2007**, *129*, 12032.
[15] Ebine, M.; Suga, Y.; Fuwa, H.; Sasaki, M. *Org. Biomol. Chem.* **2010**, *8*, 39.
[16] Emily, B. P.; Tendai, G.; Sonbinh, T. N. *Org. Lett.* **2008**, *10*, 5613.
[17] van As, B. A. C.; Chan, D.; Kivit, P. J. J.; Palmans, A. R. A.; Meijer, E. W. *Tetrahedron*: *Asymmetry* **2007**, *18*, 787.
[18] Maxime, A. S.; Huub, K.; Anthony, L. S. *Acta Cryst*. **2008**, *E64*, o607.
[19] Fukuzawa, A.; Masamune, T. *Tetrahedron Lett*. 1**981**, *22*, 4081.
[20] Cremer, D. J.; Pople, A. *J. Am. Chem. Soc*. **1975**, *97*, 1354.
[21] Wandjia, J.; Wansi, J. D.; Fuendjiep, V.; Dagne, E.; Mulholland, D. A.; Tillequin, F.; Fomum, Z. T.; Sondengam, B. L.; Nkeh, B. C.; Njamen, D. *Phytochemistry* **2000**, *54*, 811.
[22] Nkeh, B. C.; Njamen, D.; Wandjia, J.; Fomum, Z. T.; Dongmo, A.; Nguelefack, T. B.; Wansi, J. D.; Kamanyi, A. *Pharm. Biol.* **2003**, *41*, 26.
[23] Jhulki, S.; Seth, S.; Mondal, M.; Moorthy, J. N. *Tetrahedron* **2014**, *70*, 2286.
[24] Kadnikov, D. V.; Larock, R. C. *Mendeleev Commun.* **2007**, *17*, 74.
[25] Cheng, Y. A.; Chen, T.; Tan, C. K.; Heng, J. J.; Yeung, Y. Y. *J. Am. Chem. Soc*. **2012**, *134*, 16492.
[26] Wang, L.; Ren, Z.-L.; Ding, M.-W. *J. Org. Chem.* **2015**, *80*, 641.
[27] Arcadi, A.; Fabrizi, G.; Goggiamani, A.; Marinelli, F. *J. Org. Chem.* **2015**, *80*, 6986.
[28] Matsuda, T.; Shigeno, M.; Murakami, M. *Org. Lett.* **2008**, *10*, 5219.
[29] Zarrabi, S.; Mahmoodi, N.O.; Tabatabaeian, K.; Zanjanchi, M. A. *Chin. Chem. Lett.* **2009**, *20*, 1400.
[30] Dong, H. B.; Yang, M. Y.; Jiang, J. Z.; Wang, M. A. *J. Asian Nat. Prod. Res.* **2013**, *15*, 880.
[31] Dong, H. B.; Yang, M. Y.; Tang, B.; Wang, M. A. *Chin. J. Org. Chem.* **2014**, *34*, 2350 (in Chinese).
(董宏波, 杨明艳, 汤博, 王明安, 有机化学, **2014**, *34*, 2350.)
[32] Zhao, J.; Dong, H. B.; Yang, M. Y.; Du, J.; Jiang, J. Z.; Wang, M. A. *J. Asian Nat. Prod. Res.* **2014**, *16*, 312.
[33] Dong, H. B.; Wang, W. W.; Zhao, Y.; Liu, X. L.; Wang, M. A. *Chin. J. Org. Chem.* **2021**, *41*, 1646 (in Chinese).
(董宏波, 王卫伟, 赵宇, 刘鑫磊, 王明安, 有机化学, **2021**, *41*, 1646.)
[34] Yonova, I. M.; Johnson, A. G.; Osborne, C. A.; Moore, C. E.; Morrissette, N. S.; Jorvo, E. R. *Angew. Chem.*, *Int. Ed.* **2014**, *53*, 2422.
[35] Touchard, F. P. *Tetrahedron Lett.* **2004**, *45*, 5519.
[36] Wang, W. W.; Zhao, Y.; Liu, X. L.; Geng, R.; Wang, M. A. *Chin. J. Org. Chem.* **2019**, *39*, 1129 (in Chinese).
(王卫伟, 赵宇, 刘鑫磊, 耿瑞, 王明安, 有机化学, **2019**, *39*, 1129.)
[37] Tang, B.; Guan, A. Y.; Zhao, Y.; Jiang, J. Z.; Wang, M. A.; Zhou, L. G. *Chin. J. Chem.* **2017**, *35*, 1133.
[38] Zhao, Y.; Tang, B.; Guan, A. Y.; Wang, W. W.; Zhang, Z. H.; Wang, M. A. *Synthesis* **2017**, *49*, 4663.
[39] Geng, R.; Zhao, Y.; Li, Y. H.; Liu, X. L.; Wang, M. A. *Chin. J. Org. Chem.* **2019**, *39*, 3574 (in Chinese).
(耿瑞, 赵宇, 李益豪, 刘鑫磊, 王明安, 有机化学, **2019**, *39*, 3574.)
[40] Schwartz, B. D.; Tilly, D. P.; Heim, R.; Wiedemann, S.; Williams, C. M.; Bernhardt, P. V. *Eur. J. Org. Chem.* **2006**, 3181.
[41] Anastasia, L.; Dumond, Y. R.; Negishi, E. *Eur. J. Org. Chem.* **2001**, 3039.
[42] Derrick, L. J.; Clive, V. F.; Pierre, L. B. *J. Org. Chem.* **1982**, *47*, 2572.

(Cheng, F.)

