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Efficient Syntheses of Traumatic Lactone and Rhizobialide

Jing Zhou[a], Shihua Song[a], Feng Jiang[a], Chunling Fu[a], Shengming Ma*[a]

Dedication ((optional))

Abstract: Herein, we reported the total syntheses of traumatic lactone and rhizobialide via the strategy of utilizing allenoic acid to construct the lactone ring. The key starting materials, allenoic acids, could be prepared by the ATA (allenation of terminal alkynes) of a terminal alkyne with an aldehyde bearing a protected hydroxyl group followed by hydrolysis. Importantly, the asymmetric syntheses could be realized just by replacing racemic diphenylprinol with (*R*)- or (*S*)-diphenylprinol to deliver the optically active allenoate.

1. Introduction

Molecules containing γ-butyrolactone moiety extensively occur in nature and many of them have potentials as lead drug compounds [1-6] or fine chemicals releasing unique fragrance [7]. Traumatic lactone **1**, γ-(7-carboxyheptyl) γ-butyrolactone, was isolated by Masamune from *phaseolus vulgaris*, beni-kintoki.[8] Structurally very related lactone, rhizobialide **2**, was isolated from *glycyrrhiza uralensis*, and showed anti-bacterial activity against *Staphylococcus aureus* CMCCB26001 and Escherichia coli CMCCB44102.[3,9] In this paper, we wish to report our recent efforts towards the syntheses of these two naturally occurring lactones (Fig. 1).

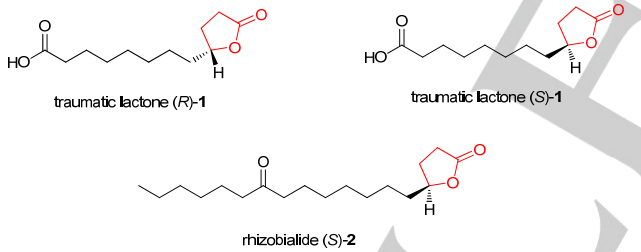


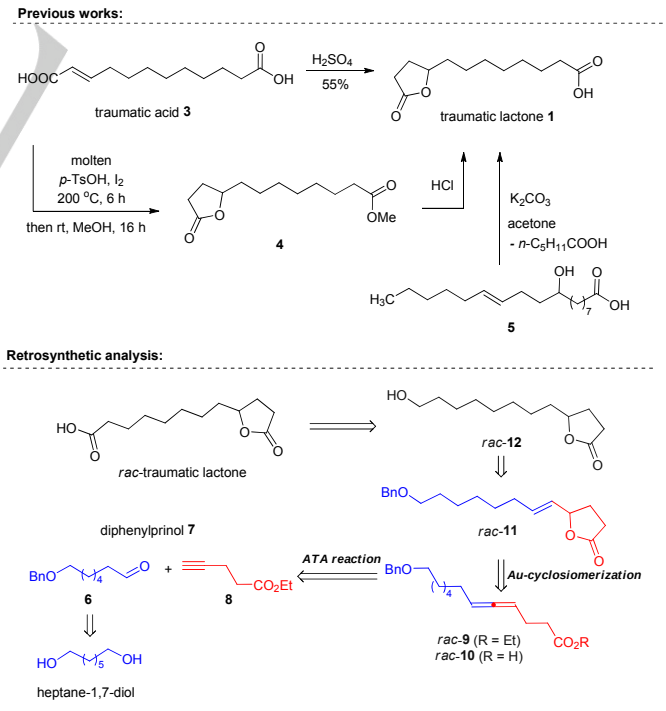
Fig. 1 The structures of traumatic lactone (*R*)/(*S*)-1 and rhizobialide (*S*)-2

2. Results and Discussion

2.1. Synthesis of *rac*-traumatic lactone

Nayak et al. prepared traumatic lactone **1** from traumatic acid **3**.[10a] Interestingly, even before the isolation from natural resource, traumatic lactone **1** was prepared in 1951 from 9-hydroxyoctadec-12-enoic acid **5**, which was isolated from the seed oil of *sarmentosus* by Gunstone, by its treatment with K_2CO_3.[10b] Sayre et al. mimicked the formation of traumatic lactone in nature.[11] It's obvious that these methods suffer from unavailable starting materials, strong acid, and high temperature. It's only lately that we reported the racemic and asymmetric syntheses of traumatic lactone[12] by Pd-catalyzed allene-asymmerization of 2,3-allenyl carbonates to produce the key allene moiety with 91% ee, and the additional recrystallization work-up was necessary to obtain excellent ee values. So there is still a need for the development of new efficient approaches to traumatic lactone, especially the asymmetric versions.

Recently, ATA (allenation of terminal alkynes)[13] reactions have emerged as a powerful method to prepare functionalized allenes. On the other hand, we have developed the strategy utilizing allenoic acid to construct lactone ring based on Au-catalysis[14,15] to modulate the control of axial-to-central chirality transfer efficiency and *Z*/*E* selectivity-the stereoselective cyclization of allenoic acid.[14b] We envisage such a strategy by combination ATA reaction with Au-catalysis could be exploited for the synthesis of traumatic lactone. The retrosynthetic analysis of traumatic lactone is shown in Scheme 1.



Scheme 1. The previous works and retrosynthetic analysis for traumatic lactone

[a] J. Zhou, S. Song, F. Jiang, C. Fu, S. Ma
Department Laboratory of Molecular Recognition and Synthesis, Department of Chemistry, Zhejiang University, 310027 Hangzhou city, Zhejiang, People's Republic of China.
E-mail: masm@sioc.ac.cn

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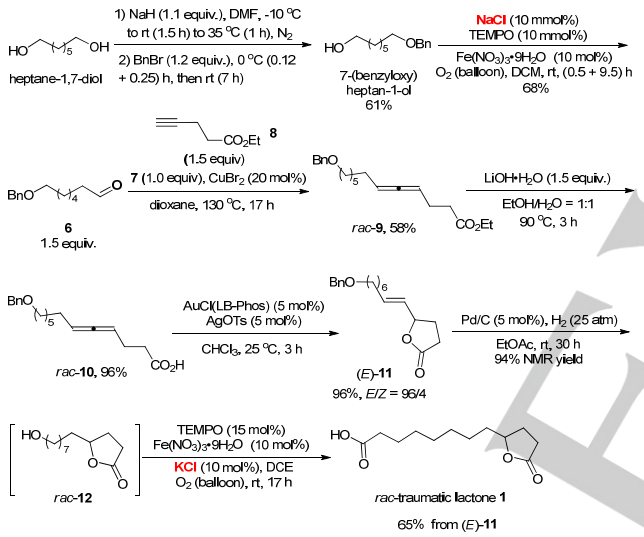
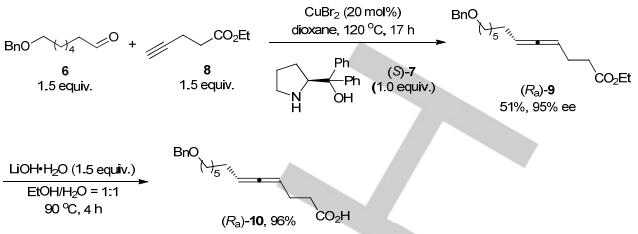
Thus, 1,7-heptandiol was treated with BnBr in the presence of NaH to afford the monoetherification product, benzoxyheptanol, in 61% yield, which was subsequently oxidized to aldehyde **6** with oxygen as the oxidant under the catalysis of $Fe(NO_3)_3{\cdot}9H_2O$, TEMPO, and NaCl[16a] (Scheme 2). ATA reaction of ethyl 4-pentynoate **8** and aldehyde **6** in the presence of diphenylprinol afforded allenoate *rac*-**9**,[13] which was hydrolyzed to afford allenoic acid *rac*-**10**. Its AuCl(LB-Phos)-catalyzed cyclziation[14b] afford *E*-alkenyl lactone (*E*)-**11** with a *E*/*Z* selectivity of 96:4. The C=C bond and benzyl ether unit in this product were hydrogenated and cleaved simultaneously to afford lactone *rac*-**12** with a terminal primary alcohol unit. Under the catalysis of 5 mol% Pd/C, the reaction of (*E*)-**10** in ethyl acetate with 25 atm H_2 for 36 h would led to the formation lactone ring opening product, therefore, the reaction time was shortened to 30 h to afford *rac*-**12** in 94% NMR yield exclusively. Subsequent aerobic oxidation with KCl[16b,c] afforded the racemic traumatic acid **1**.



Scheme 2. The synthesis of (±) traumatic lactone

2.2. Synthesis of (*R*)- and (*S*)-traumatic lactones

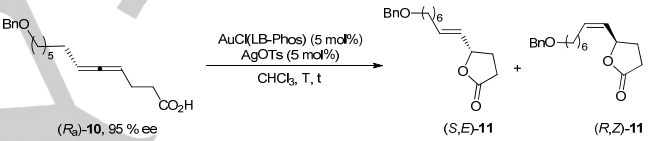
With a synthetic route being developed for racemic traumatic lactone **1**, the enantioselective synthesis of (*R*)-traumatic lactone was conducted just by replacing racemic diphenylprinol with (*S*)-diphenylprinol **7** to deliver the optically active allenoate (R_a)-**9**, which was hydrolyzed to afford allenoic acid (R_a)-**10** (Scheme 3). However, owing to the existence of free carboxylic acid group, the direct analysis of (R_a)-**10** by HPLC analysis is difficult but not obligatory. The following results witnessed the hydrolysis by $LiOH{\cdot}H_2O$ had no damage on the ee value.



Scheme 3. The synthesis of (R_a)-9 and (R_a)-10.

After hydrolysis, the cycloiosmerization of optically active allenioc acid (R_a)-**10** was optimized to ensure the efficiency of chirality transfer and a high *E*/*Z* selectivity (Table 1). The optimal cyclization reaction conditions at -20 °C led to the formation of (*S*,*E*)-**11** in 96% ee with a *E*/*Z* selectivity of 98:2.

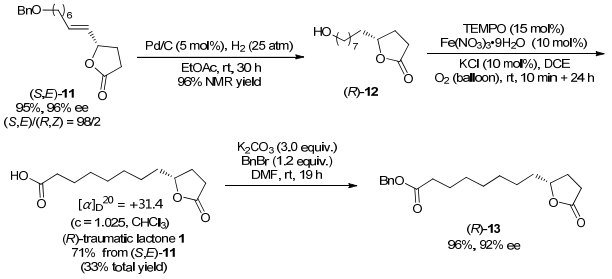
Table 1. Optimization of the reaction conditions for the cyclization of (R_a)-10[a].



Entry	T/°C	t/h	11			Recovery of (R_a)-10/%[b]
			Yield/% [b]	(*S*,*E*)/(*R*,*Z*) [b]	ee%[c]	
1	25	2	100	96:4	96	0
2	0	11	100	97:3	95	0
3	**-20**	**12**	**100**	**98:2**	**96**	**0**
4	-40	36	75	98:2	-	23

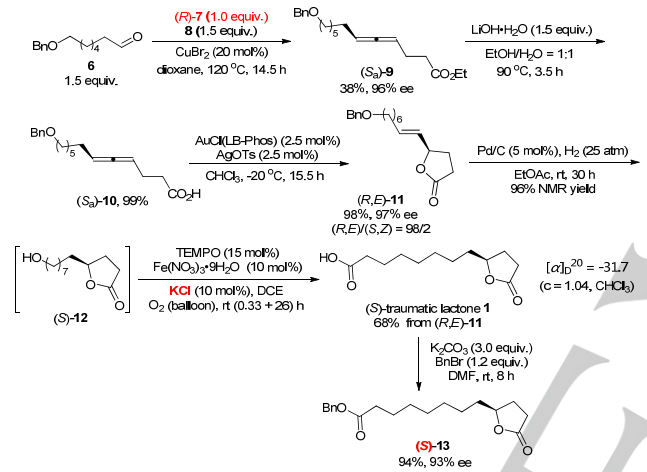
[a] AgOTs (0.01 mmol), AuCl(LB-Phos) (0.01 mmol), and $CHCl_3$ (2 mL) were stirred at room temperature for 15 min under nitrogen atmosphere; then 0.2 mmol of (R_a)-**10** and $CHCl_3$ (1 mL) were added. [b] Determined by ^1H NMR of crude product using 1,3,5-trimethylbenzene as internal standard. [c] ee % of (*S*,*E*)-**11**; Determined by chiral high-performance liquid chromatography (HPLC) analysis.

Finally, after hydrogenation and subsequent aerobic oxidation, the (*R*)-traumatic acid (*R*)-**1** was afforded in 33% combined yield. Upon converting it to its benzyl ester (*R*)-**13**, the ee value of (*R*)-traumatic lactone was identified as 92% (Scheme 4).



Scheme 4. The asymmetric synthesis of (*R*)-traumatic lactone.

In addition, we also synthesized (*S*)-traumatic lactone with a similar efficiency and ee by replacing amino alcohol (*S*)-**7** with (*R*)-**7** (Scheme 5).

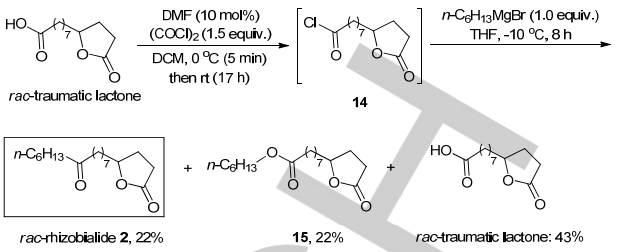


Scheme 5. The asymmetric synthesis of (*S*)-traumatic lactone.

2.3. Synthesis of rhizobialide

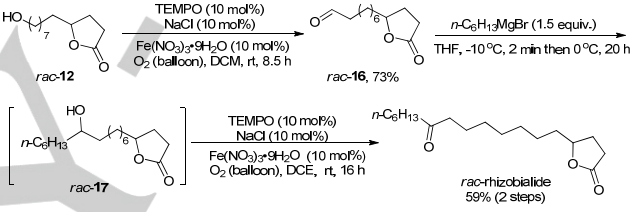
2.3.1. Synthesis of *rac*-rhizobialide

There is only one report on its synthesis from glutamic acid with 8 steps.[17] Due to the similarity of rhizobialide as compared to traumatic lactone, we tried to prepare rhizobialide from traumatic lactone. At 0 °C, the solution of *rac*-traumatic lactone in CH_2Cl_2 was treated with 10 mol% anhydrous DMF and 1.5 equiv of freshly distilled $(COCl)_2$. After 17 h at rt, the free carboxylic acid group was converted to the corresponding acyl chloride **14**, which was subsequently treated with *n*-C_6H_{13}MgBr in THF at -10 °C for 8 h[18] to afford 22% isolated yield of *rac*-rhizobialide **2** together with 22% lactonyl ester **15** as an inseparable mixture. Moreover, *rac*-Traumatic lactone was recovered in 43% yield (Scheme 6).



Scheme 6. The synthesis of *rac*-rhizobialide 2 from *rac*-traumatic lactone 1.

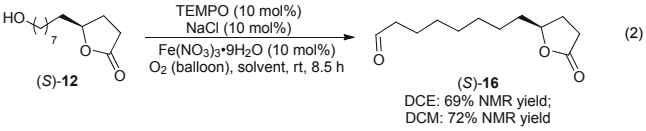
In order to have a highly selective synthesis, we considered to use alcohol **12** as the starting point. We conducted the aerobic oxidation of primary alcohol *rac*-**12** to aldehyde *rac*-**16**. The reaction of *rac*-**16** with *n*-C_6H_{13}MgBr afforded secondary alcohol *rac*-**17**, which was oxidized with oxygen to afford *rac*-rhizobialide **2**[16] (Scheme 7).



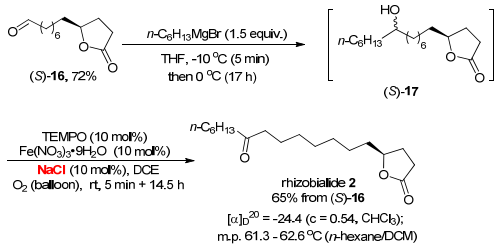
Scheme 7. The synthesis of *rac*-rhizobialide 2 from primary alcohol.

2.3.2. Synthesis of (*S*)-rhizobialide

Under the catalysis of 10 mol% $Fe(NO_3)_3 \cdot 9H_2O$, 10 mol% TEMPO, and 10 mol% NaCl, the aerobic oxidation reaction of (*S*)-**12** in 1,2-dichloroethane afforded aldehyde (*S*)-**16** in 69% NMR yield; the NMR yield of (*S*)-**16** was improved to 72% when the reaction was conducted in CH_2Cl_2 (eq. 2).



The reaction of aldehyde (*S*)-**16** with *n*-C_6H_{13}MgBr afforded secondary (*S*)-**17**, which was further oxidized with oxygen to afford 65% yield of rhizobialide (*S*)-**2**: the whole synthesis took 7 steps from aldehyde **6** to afford the target in 19.4%: $[a]_D^{20}$ = -24.4 (c = 0.54, $CHCl_3$) (ref.: $[a]_D^{20}$ = -19.7 (c = 0.55, $CHCl_3$) (Scheme 8).



Scheme 8. The asymmetric synthesis of rhizobialide (*S*)-2.

3. Conclusion

In conclusion, allenylation of terminal alkynoate with 7-benzoxyheptanal in the presence of (*S*)- or (*R*)-diphenylprinol, AuCl(LB-Phos)-catalyzed highly stereoselective cycloisomerization of allenoic acid and $Fe(NO_3)_3{\cdot}9H_2O$ /TEMPO/MCl-catalyzed aerobic oxidation have been applied as the key technology for efficient (enantioselective) syntheses of the naturally occurring traumatic lactone and rhizobialide. Further synthetic application of these reactions is being pursued in our laboratory.

4. Experimental Section

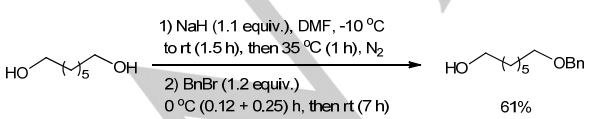
4.1. General

^1H and ^{13}C nuclear magnetic resonance spectra were recorded with an instrument operated at 300 MHz for ^1H NMR spectra and 75 MHz for ^{13}C NMR spectra. $CDCl_3$ was used as solvent in all NMR experiments. Chemical shifts (δ) are given in parts per million (ppm). Infrared spectra were recorded from the films of pure samples on sodium chloride plates on a FT-IR spectrometer. Mass and HRMS spectra were carried out in EI mode. Flash column chromatography was performed on silica gel. Dioxane and THF were refluxed over sodium wire using diphenyl ketone as indicator and distilled right before use. $CuBr_2$ was purchased from J & K. (*S*)-α,α-diphenylprolinol and (*R*)-α,α-diphenylprolinol were purchased from Shanghai Darui Fine Chemicals. AgOTs was purchased from Alfa Aesar. Other commercially available reagents were purchased and used without further purification.

4.2. Synthesis of traumatic lactones

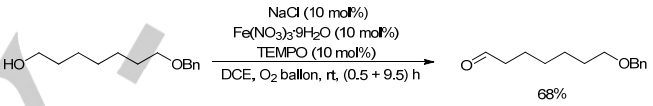
4.2.1. Synthesis of *rac*-traumatic lactone

4.2.1.1. Synthesis of 7-(benzyloxy)heptan-1-ol (zj-8-127)



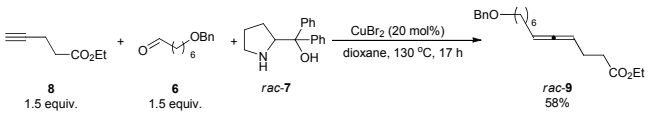
To a flame-dried three-necked flask with an addition funnel were added NaH (4.4174 g, purity = 60% in mineral oil, 110 mmol) and DMF (150 mL) sequentially at rt under nitrogen atmosphere. Then the resulting mixture was cooled to -10 °C and a solution of heptane-1,7-diol (13.8975 g, purity = 95%, 100 mmol) in DMF (50 mL) was added quickly. The resulting mixture was warmed up to rt gradually and reacted for another 1.5 h and then at 35 °C for 1 h. The resulting mixture was cooled with an ice-water bath for 5 minutes and BnBr (14.3 mL, d = 1.44 g/mL, 20.592 g, 120 mmol) was added dropwise within 15 minutes. Subsequently, the flask was warmed up to rt gradually. The reaction was complete after being stirred at rt for 7 h as monitored by TLC and quenched with H_2O (100 mL). After stirring for 10 minutes, the reaction mixture was extracted with ethyl acetate (40 mL × 5). The combined organic layer was washed with water, brine and dried over anhydrous Na_2SO_4. After filtration and evaporation, the residue was purified by chromatography on silica gel [eluent: petroleum ether (60-90 °C)/ethyl acetate = 100/1 (500 mL) to 50/1 (1000 mL) to 30/1 (1000 mL) to 20/1 (500 mL) to 10/1 (500 mL) to 8/1 (500 mL) to 5/1 (600 mL) to 1/1 (600 mL)] on silica gel to afford 7-(benzyloxy)heptan-1-ol[19] (13.5661 g, 61%) as a liquid: ^1H NMR (300 MHz, $CDCl_3$) δ 7.38-7.23 (m, 5H, ArH), 4.49 (s, 2H, OCH_2), 3.58 (t, *J* = 6.5 Hz, , 2H, OCH_2), 3.46 (t, *J* = 6.5 Hz, 2H, OCH_2), 1.94 (s, 1H, OH), 1.67-1.46 (m, H, CH_2 × 2), 1.44-1.27 (m, 6H, CH_2 × 3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.5, 128.2, 127.5, 127.4, 72.7, 70.3, 62.7, 32.5, 29.6, 29.1, 26.0, 25.6.

4.2.1.2. Synthesis of 7-(benzyloxy)heptanal 6 (zj-9-063)



Typical Procedure I :[16] To a three-necked flask were added $Fe(NO_3)_3{\cdot}9H_2O$ (1.7105 g, purity = 98%, 4.2 mmol), NaCl (0.2437 g, 4.2 mmol), TEMPO (0.6688 g, purity = 98%, 4.2 mmol), and DCE (320 mL) sequentially. An oxygen balloon was equipped followed by dropwise addition of a solution of 7-(benzyloxy)heptan-1-ol in 100 mL of DCE at room temperature within 0.5 h in oxygen atmosphere from the balloon. The resulting mixture was stirred for 9.5 h until the reaction was complete as monitored by TLC. After transfer to a separation funnel, the organic phase was washed with 3 M HCl (aq., 30 mL × 3), a saturated solution of $NaHCO_3$ (30 mL), brine sequentially, and dried over anhydrous Na_2SO_4. After filtration and evaporation, the residue was purified by chromatography on silica gel [eluent: petroleum ether (60-90 °C)/ethyl acetate = 50/1 (500 mL) to 30/1 (480 mL) to 20/1 (500 mL) to 10/1 (1040 mL) to 5/1 (300 mL) to afford 7-(benzyloxy)heptanal **6**[19] (7.1345 g, 68%) as a liquid: ^1H NMR (300 MHz, $CDCl_3$) 9.75 (t, *J* = 1.8 Hz, 1H, CHO), 7.38-7.23 (m, 5H, ArH), 4.50 (s, 2H, OCH_2), 3.46 (t, 2H, *J* = 6.5 Hz, OCH_2), 2.41 (td, J_1 = 7.3 Hz, J_2 = 1.7 Hz, 2H, CH_2), 1.68-1.55 (m, 4H, CH_2 × 2), 1.46-1.27 (m, 4H, CH_2 × 2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.7, 138.5, 128.3, 127.5, 127.4, 72.8, 70.1, 43.7, 29.5, 28.9, 25.9, 21.9.

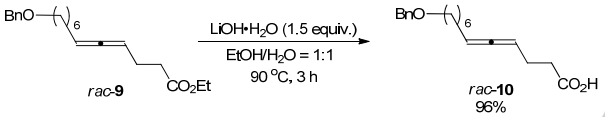
4.2.1.3. Synthesis of ethyl 12-(benzyloxy)dodeca-4,5-dienoate *rac*-**9** (zj-8-085, jf-1-009)



Typical Procedure II : To a flame-dried Schlenk tube with a polytetrafluoroethylene plug were added $CuBr_2$ (0.1353 g, 0.6 mmol, 99%), *rac*-2-(diphenylhydroxymethyl)pyrrolidine *rac*-**7** (0.7744 g, 3.0 mmol, 98%), ethyl pent-4-ynoate **8** (0.5678 g, 4.5 mmol)/dioxane (2.5 mL), and 7-(benzyloxy)heptanal **6** (0.9902 g, 4.5 mmol)/dioxane (2.5 mL) sequentially under nitrogen atmosphere. The Schlenk tube was then sealed by screwing the polytetrafluoroethylene plug tightly. The reaction

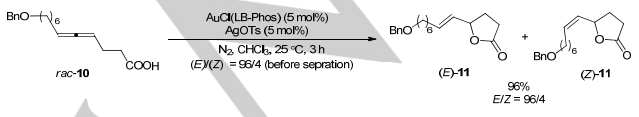
was complete after being stirred in an oil bath preheated at 130 °C for 17 h as monitored by TLC. The resulting mixture was cooled to room temperature, diluted with Et_2O (30 mL), and washed with an aqueous solution of hydrochloric acid (10 mL, 3 M). The organic layer was separated and the aqueous layer was extracted with Et_2O (10 mL). The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. After filtration and evaporation, the residue was purified by chromatography on silica gel [eluent: petroleum ether (60-90 °C)/ethyl acetate = 100/1 (500 mL) to 50/1 (500 mL) to 30/1 (500 mL)] to afford *rac*-**9**[13] (0.5930 g, 58%) as a liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40-7.20 (m, 5H, ArH), 5.19-5.06 (m, 2H, =CH × 2), 4.49 (s, 2H, $ArCH_2$), 4.12 (q, *J* = 7.0 Hz, 2H, CH_2), 3.46 (t, *J* = 6.6 Hz, 2H, CH_2), 2.44-2.35 (m, 2H, CH_2), 2.34-2.23 (m, 2H, CH_2), 2.02-1.89 (m, 2H, CH_2), 1.67-1.54 (m, 2H, CH_2), 1.45-1.27 (m, 6H, CH_2 × 3), 1.24 (t, *J* = 7.1 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.5, 172.8, 138.5, 128.1, 127.3, 127.2, 92.2, 89.4, 72.6, 70.2, 60.0, 33.2, 29.5, 28.8, 28.7, 28.6, 25.8, 23.7, 14.0; IR (neat) ν (cm^{-1}) 3092, 3064, 3030, 2976, 2931, 2855, 2791, 1962, 1732, 1496, 1454, 1371, 1301, 1250, 1158, 1100, 1028; MS (70 ev, EI) *m/z* (%) 331 (M^++1, 5.01), 330 (M^+, 7.89), 91 (100); HRMS calcd for $C_{21}H_{30}O_3$ [M^+]: 330.2195, Found: 330.2199.

4.2.1.4. Synthesis of 12-(benzyloxy)dodeca-4,5-dienoic acid *rac*-**10** (zj-8-086, jf-1-010)



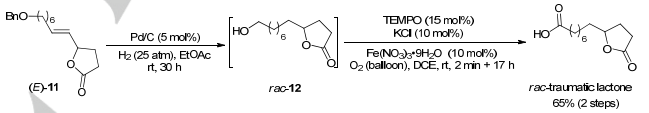
Typical Procedure III: To a round-bottom flask were added *rac*-**9** (0.5331 g, 1.62 mmol), EtOH/H_2O = 1:1 by volume (pre-mixed by using 8 mL of H_2O and 8 mL of EtOH), and $LiOH·H_2O$ (0.1075 g, 2.43 mmol, 95%) sequentially. After continuous stirring for 3 h under reflux at 90 °C, the reaction was complete as monitored by TLC. Then the mixture was cooled to room temperature. After evaporation to remove EtOH, the resulting mixture was acidified with an aqueous solution of hydrochloric acid (aq., 3.0 M) until pH = 1 and then extracted with Et_2O (15 mL × 3). The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtration, evaporation, and column chromatography on silica gel to give *rac*-**10** (0.4671 g, 96%) [eluent: petroleum ether (60-90 °C)/ ethyl acetate = 10/1 (550 mL) to 5:1 (600 mL) to 3:1 (240 mL)] as an oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.28 (bs, 1H, COOH), 7.43-7.22 (m, 5H, ArH), 5.22-5.09 (m, 2H, =CH × 2), 4.51 (s, 2H, $ArCH_2$), 3.46 (t, *J* = 6.6 Hz, 2H, CH_2), 2.52-2.41 (m, 2H, CH_2), 2.35-2.22 (m, 2H, CH_2), 2.02-1.89 (m, 2H, CH_2), 1.68-1.55 (m, 2H, CH_2), 1.46-1.24 (m, 6H, CH_2 × 3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.7, 178.7, 138.5, 128.3, 127.7, 127.5, 92.8, 89.4, 72.8, 70.4, 33.0, 29.6, 28.9, 28.8, 28.7, 25.9, 23.5; IR (neat) ν (cm^{-1}) 3686-2142 (COOH), 1963, 1714, 1496, 1455, 1361, 1251, 1208, 1160, 1100, 1028; MS (70 ev, EI) *m/z* (%) 303 (M^++1, 37.01), 302 (M^+, 3.92), 91 (100); HRMS calcd for $C_{19}H_{26}O_3$ [M^+]: 302.1882, Found: 302.1882.

4.2.1.5. Synthesis of (*E*)-5-(8-(benzyloxy)oct-1-en-1-yl)dihydro-2(3*H*)-furanone (*E*)-**11** (zj-8-089)



Typical Procedure IV:[14b] To a dried Schlenk tube were added AgOTs (0.0171 g, 0.06 mmol, weighed in a glove box, 98%), AuCl(LB-Phos) (0.0358 g, 0.06 mmol), and $CHCl_3$ (6 mL) under nitrogen atmosphere sequentially. After stirring for 15 min, *rac*-**10** (0.3616 g, 1.2 mmol) and $CHCl_3$ (6 mL) were added. The reaction mixture was then continuously stirred at 25 °C for 3 h and complete as monitored by TLC. Filtration through a short column of silica gel [eluent: Et_2O (20 mL × 3)] and evaporation afforded a crude mixture of (*E*)-**11** and (*Z*)-**11** (*E*/*Z* = 96/4, as determined by ^{1}H NMR analysis). Column chromatography on silica gel afforded (*E*)-**11** (0.3479 g, 96%, *E*/*Z* = 96/4 as determined by ^{1}H NMR analysis) [eluent: petroleum ether (60-90 °C)/ethyl acetate = 15/1 (480 mL) to 10/1 (550 mL) to 7/1 (400 mL)] as an oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38-7.20 (m, 5H, ArH), 5.78 (dtd, J_1 = 15.3 Hz, J_2 = 6.9 Hz, J_3 = 0.9 Hz, 1H, =CH), 5.47 (ddt, J_1 = 15.3 Hz, J_2 = 7.2 Hz, J_3 = 1.4 Hz, 1H, =CH), 4.85 (q, *J* = 7.1 Hz, 1H, CH), 4.49 (s, 2H, CH_2), 3.46 (t, *J* = 6.5 Hz, 2H, CH_2), 2.53-2.45 (m, 2H, CH_2), 2.39-2.26 (m, 1H, one proton from CH_2), 2.05 (q, *J* = 6.7 Hz, 2H, CH_2), 2.00-1.85 (m, 1H, one proton from CH_2), 1.66-1.53 (m, 2H, CH_2), 1.45-1.23 (m, 6H, CH_2 × 3); the following signals are discernible for (*Z*)-**6**: δ 5.69-5.59 (m, 1H, =CH), 5.26-5.16 (m, 1H, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.9, 138.5, 135.3, 128.1, 127.4, 127.3, 127.2, 80.9, 72.6, 70.2, 31.8, 29.4, 28.7, 28.6, 28.5, 25.8; IR (neat) ν (cm^{-1}) 3087, 3061, 3030, 2930, 2855, 2792, 1770, 1673, 1496, 1455, 1362, 1327, 1216, 1175, 1102, 1008; GC-MS (GC condition: injector: 280 °C; column: DB5 column 30 m × 0.25 mm, temperature programming: 60 °C (2 min), 20 °C/min to 280 °C, 280 °C (30 min); detector: 280 °C) (70 ev, EI) *m/z* (%) for (*E*)-**11**: t_R (major) = 9.36 min: 302 (M^+, 0.38), 193 [(M - C_7H_9O)$^+$, 14.03], 91 (100); for (*Z*)-**11**: t_R (minor) = 9.14 min: 302 (M^+, 0.12), 193 [(M - C_7H_9O)$^+$, 8.64], 91 (100); Elemental analysis calcd (%) for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67; Found: C, 75.11; H, 8.63.

4.2.1.6. Synthesis of *rac*-traumatic lactone (zj-8-095, zj-8-097)



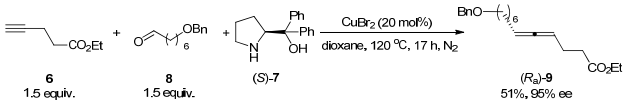
Typical Procedure V: To a round-bottom flask were added (*E*)-**11** (*E*/*Z* = 96/4) (0.3021 g, 1.0 mmol), EtOAc (6 mL), and Pd/C (10% on C, dry, 0.0533 g, 0.05 mmol) sequentially. Then the flask was placed in an autoclave. The mixture was stirred under H_2 (25 atm) at rt for 30 h and then filtered through a short column of silica gel eluted with EtOAc (15 mL × 4). After evaporation, crude *rac*-**12**[20] (94% NMR yield, determined by ^{1}H NMR of crude product using 1,3,5-trimethylbenzene as internal standard) was afforded, which was then submitted to next step without purification.

Following **Typical Procedure I:**[16] To a three-necked flask were added $Fe(NO_3)_3·9H_2O$ (0.0406 g, 0.1 mmol, 98%), KCl (0.0075 g, 0.1 mmol), TEMPO (0.0239 g, 0.15 mmol, 98%), alcohol *rac*-**12** (prepared above), and DCE (5 mL) sequentially. The resulting mixture was stirred at rt for 17 h until the reaction was complete as monitored by TLC. After filtration through a short column of silica gel [eluent: DCM (10 mL × 4)] and evaporation, the residue was purified by chromatography on silica gel [eluent: petroleum ether (60-90 °C)/ethyl acetate = 5/1 (600 mL) to 3/1 (600 mL) to 2/1 (800 mL)] to afford *rac*-traumatic lactone (0.1471 g, 65%, 2 steps) as a white solid: m. p. 53.9-55.1 °C (*n*-hexane/dichloromethane) (Lit.[8] m. p. 48.5-50 °C (isopropyl ether/*n*-hexane)); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.03 (bs, 1H, COOH), 4.51 (quintet, *J* = 7.2 Hz, 1H, OCH), 2.62-2.48 (m, 2H, CH_2), 2.43-2.25 (m, 3H, CH_2 + one proton from CH_2), 1.96-1.53 (m, 5H, CH_2 × 2 + one proton from CH_2), 1.53-1.22 (m, 8H, CH_2 × 4); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.3, 177.5, 80.9, 35.1, 33.7, 28.72, 28.68, 28.6, 28.5, 27.6, 24.8, 24.2; IR (neat) ν (cm^{-1}) 3716-2218

(COOH), 1771, 1711, 1461, 1420, 1356, 1284, 1186, 1017; MS (70 ev, EI) *m/z* (%) 229 (M^+ + 1, 19.74), 228 (M^+, 1.81), 211 (100), 85 (100).

4.2.2. Total synthesis of (*R*)-traumatic lactone

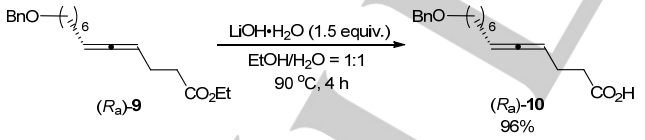
4.2.2.1. Synthesis of ethyl (R_a)-12-(benzyloxy)dodeca-4,5-dienoate (R_a)-**9** (zj-8-088, jf-1-012)



6 1.5 equiv. **8** 1.5 equiv. (*S*)-**7** (R_a)-**9** 51%, 95% ee

Typical Procedure VI: To a dry Schlenk flask were added $CuBr_2$ (0.4958 g, 2.2 mmol, 99%), (*S*)-**7** (2.8396 g, 11 mmol, 98%), **8** (2.0787 g, 16.5 mmol)/dioxane (20 mL), and **6** (3.6311 g, 16.5 mmol)/dioxane (13 mL) sequentially under nitrogen atmosphere. After continuous stirring for 17 h under reflux at 120 °C, the reaction was complete as monitored by TLC. The resulting mixture was cooled to room temperature. The mixture was diluted with ether (90 mL) and then washed with an aqueous solution of hydrochloric acid (3 M, 15 mL × 3). The organic layer was separated and the aqueous layer was extracted with Et_2O (20 mL). The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. After filtration and evaporation, the residue was purified by chromatography on silica gel [eluent: petroleum ether (60-90 °C)/ethyl acetate = 100/1 (300 mL) to 50:1 (300 mL) to 30:1 (500 mL) to 20:1 (500 mL) to 10:1 (500 mL)] to afford (R_a)-**9** (1.8645 g, 51%) as an liquid: 95% ee (HPLC conditions: Chiralcel AS-H column, *n*-hexane/*i*-PrOH = 100:1, 1.0 mL/min, λ = 214 nm, t_R (major) = 17.2 min, t_R (minor) = 18.8 min; $[\alpha]_D^{20}$ = -49.2 (*c* = 1.005, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42-7.21 (m, 5H, ArH), 5.19-5.07 (m, 2H, =CH × 2), 4.49 (s, 2H, $ArCH_2$), 4.11 (q, *J* = 7.1 Hz, 2H, CH_2), 3.45 (t, *J* = 6.5 Hz, 2H, CH_2), 2.44-2.35 (m, 2H, CH_2), 2.34-2.22 (m, 2H, CH_2), 2.01-1.89 (m, 2H, CH_2), 1.67-1.55 (m, 2H, CH_2), 1.45-1.28 (m, 6H, CH_2 × 3), 1.24 (t, *J* = 7.2 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.5, 172.9, 138.5, 128.2, 127.4, 127.3, 92.2, 89.4, 72.7, 70.2, 60.1, 33.3, 29.6, 28.9, 28.8, 28.6, 25.9, 23.7, 14.1; IR (neat) ν (cm^{-1}) 3088, 3067, 3028, 2972, 2932, 2855, 2787, 1962, 1738, 1496, 1454, 1371, 1300, 1253, 1203, 1159, 1100, 1028; MS (70 ev, EI) *m/z* (%) 331 (M^++1, 2.40), 330 (M^+, 5.77), 91 (100); HRMS calcd for $C_{21}H_{30}O_3$ [M^+]: 330.2195, Found: 330.2193.

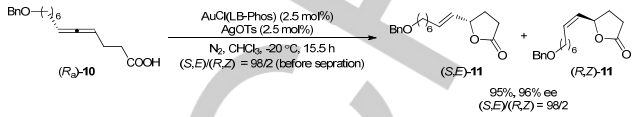
4.2.2.2. Synthesis of (R_a)-12-(benzyloxy)dodeca-4,5-dienoic acid (R_a)-**10** (zj-8-090, jf-1-013)



(R_a)-**9** (R_a)-**10** 96%

Following **Typical Procedure III**, the reaction of (R_a)-**9** (1.7655 g, 5.35 mmol), EtOH/H_2O = 1:1 by volume (pre-mixed by using 27 mL of H_2O and 27 mL of EtOH), and LiOH·H_2O (0.3550 g, 8.025 mmol, 95%) for 4 h afforded (R_a)-**10** (1.5523 g, 96%) [(eluent: petroleum ether (60-90 °C)/ethyl acetate = 15/1 (300 mL) to 10/1 (550 mL) to 5/1 (600 mL)] as an oil: $[\alpha]_D^{20}$ = -35.5 (c = 1.005, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.47 (bs, 1H, COOH), 7.40-7.23 (m, 5H, ArH), 5.19-5.09 (m, 2H, =CH × 2), 4.51 (s, 2H, $ArCH_2$), 3.46 (t, *J* = 6.6 Hz, 2H, CH_2), 2.46 (t, *J* = 7.1 Hz, 2H, CH_2), 2.34-2.23 (m, 2H, CH_2), 2.02-1.90 (m, 2H, CH_2), 1.67-1.55 (m, 2H, CH_2), 1.45-1.24 (m, 6H, CH_2 × 3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.6, 178.9, 138.5, 128.3, 127.6, 127.5, 92.7, 89.3, 72.8, 70.4, 33.0, 29.5, 28.9, 28.8, 28.7, 25.9, 23.5; IR (neat) ν (cm^{-1}) 3699-2268 (COOH), 1963, 1710, 1496, 1454, 1363, 1250, 1207, 1160, 1101, 1028; MS (70 ev, EI) *m/z* (%) 303 (M^++1, 10.72), 302 (M^+, 2.49), 91 (100); HRMS calcd for $C_{19}H_{26}O_3$ [M^+]: 302.1882, Found: 302.1885.

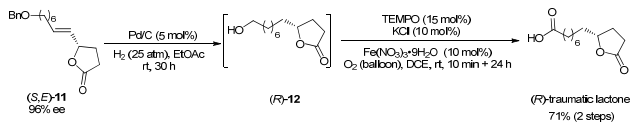
4.2.2.3. Synthesis of (*S*,*E*)-5-(8-(benzyloxy)oct-1-en-1-yl)dihydro-2(3*H*)-furanone (*S*,*E*)-**11** (zj-8-096)



(R_a)-**10** (*S*,*E*)-**11** (*R*,*Z*)-**11**
95%, 96% ee
(*S*,*E*)/(*R*,*Z*) = 98/2

Typical Procedure VII: To a dry Schlenk tube were added AgOTs (0.0214 g, 0.075 mmol, weighed in a glove box, 98%), Au(LB-Phos)Cl (0.0448 g, 0.075 mmol), and $CHCl_3$ (15 mL) under nitrogen atmosphere sequentially. After stirring at room temperature for 15 min, the reaction was cooled down to -20 °C and then (R_a)-**10** (0.9063 g, 3.0 mmol) and $CHCl_3$ (15 mL) were added. The reaction mixture was then continuously stirred at -20 °C for 15.5 h as monitored by TLC. The reaction was then warmed up to room temperature, filtration through a short column of silica gel [eluent: Et_2O (30 mL × 3)], and evaporation to afford a crude mixture of (*S*,*E*)-**11** and (*R*,*Z*)-**11** ((*S*,*E*)/(*R*,*Z*) = 98/2 determined by ^{1}H NMR of crude product). Column chromatography on silica gel [eluent: petroleum ether (60-90 °C)/ethyl acetate = 15/1 (480 mL) to 10/1 (550 mL) to 8/1 (540 mL) to 7/1 (640 mL)] afforded (*S*,*E*)-**11** (0.8647 g, 95%, (*S*,*E*)/(*R*,*Z*) = 98/2 determined by ^{1}H NMR) as an oil: 96% ee (HPLC conditions: Chiralcel PA-2 column, *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, λ = 214 nm, t_R (major) = 34.3 min, t_R (minor) = 52.3 min; $[\alpha]_D^{20}$ = +21.2 (*c* = 1.045, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38-7.20 (m, 5H, ArH), 5.84-5.71 (m, 1H, =CH), 5.46 (ddt, J_1 = 15.5 Hz, J_2 = 7.2 Hz, J_3 = 1.4 Hz, 1H, =CH), 4.84 (q, *J* = 7.1 Hz, 1H, CH), 4.48 (s, 2H, OCH_2), 3.45 (t, *J* = 6.6 Hz, 2H, CH_2), 2.54-2.44 (m, 2H, CH_2), 2.39-2.24 (m, 1H, one proton from CH_2), 2.05 (q, *J* = 6.7 Hz, 2H, CH_2), 2.00-1.83 (m, 1H, one proton from CH_2), 1.67-1.53 (m, 2H, CH_2), 1.45-1.22 (m, 6H, CH_2 × 3); the following signals are discernible for (*R*,*Z*)-**11**: δ 5.68-5.58 (m, 1H, =CH), 5.26-5.15 (m, 1H, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.8, 138.4, 135.2, 128.1, 127.32, 127.28, 127.2, 80.8, 72.6, 70.1, 31.7, 29.4, 28.6, 28.5, 28.4, 25.7; IR (neat) ν (cm^{-1}) 3087, 3062, 3030, 2929, 2853, 2791, 1774, 1671, 1496, 1453, 1364, 1327, 1175, 1101; GC-MS (GC condition: injector: 280 °C; column: DB5 column 30 m × 0.25 mm, temperature programming: 60 °C (2 min), 20 °C/min to 280 °C, 280 °C (30 min); detector: 280 °C) (70 ev, EI) *m/z* (%) for (*S*,*E*)-**11**: t_R (major) = 9.30 min: 302 (M^+, 0.15), 193 [(M - C_7H_9O)$^+$, 7.81], 91 (100); for (*R*,*Z*)-**11**: t_R (minor) = 9.11 min: 193 [(M - C_7H_9O)$^+$, 7.33], 91 (100); Elemental analysis calcd (%) for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67; Found: C, 75.19; H, 8.53.

4.2.2.4. Synthesis of (*R*)-traumatic lactone (zj-8-098, zj-8-099)



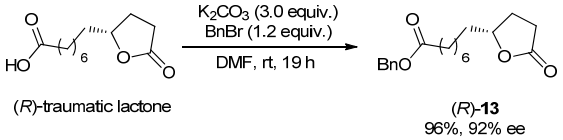
(*S*,*E*)-**11** 96% ee (*R*)-**12** (*R*)-traumatic lactone 71% (2 steps)

Following **Typical Procedure V**, the reaction of (*S*,*E*)-**11** ((*S*,*E*)/(*R*,*Z*) = 98/2) (0.7242 g, 2.4 mmol)/EtOAc (14.5 mL) and Pd/C (10% on C, dry, 0.1277 g, 0.12 mmol) for 30 h afforded crude (*R*)-**12** (96% NMR yield, determined by ^{1}H NMR of crude product using 1,3,5-trimethylbenzene as internal standard), which was submitted to next step without further characterization.

Following **Typical Procedure I**, the reaction of $Fe(NO_3)_3$·$9H_2O$ (0.0980 g, 0.24 mmol, 98%), KCl (0.0179 g, 0.24 mmol), TEMPO (0.0573 g, 0.36

mmol, 98%), DCE (5 mL), and (*R*)-**12** (prepared above)/DCE (7 mL) for 24 h afforded (*R*)-traumatic lactone (0.3881 g, 71%) [eluent: petroleum ether (60-90 °C)/ethyl acetate = 5/1 (600 mL) to 4/1 (500 mL) to 3/1 (540 mL) to 2/1 (900 mL)] as a white solid: m. p. 63.6-65.4 °C (*n*-hexane/dichloromethane); $[\alpha]_D^{20}$ = +31.4 (*c* = 1.025, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.88 (bs, 1H, COOH), 4.50 (quintet, *J* = 6.8 Hz, 1H, CH), 2.55 (dd, J_1 = 9.4 Hz, J_2 = 6.9 Hz, 2H, CH_2), 2.41-2.26 (m, 3H, CH_2 + one proton from CH_2), 1.95-1.52 (m, 5H, CH_2 × 2 + one proton from CH_2), 1.52-1.24 (m, 8H, CH_2 × 4); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.3, 177.5, 80.9, 35.1, 33.7, 28.73, 28.69, 28.6, 28.5, 27.6, 24.8, 24.2; IR (neat) ν (cm^{-1}) 3728-2284 (COOH), 1770, 1708, 1462, 1420, 1356, 1185, 1017; MS (70 ev, EI) *m/z* (%) 229 (M^+ + 1, 13.81), 228 (M^+, 0.63), 221 [(M - OH)$^+$, 88.79], 85 (100); Elemental analysis calcd (%) for $C_{12}H_{20}O_4$: C, 63.14; H, 8.83; Found: C, 63.07; H, 8.64.

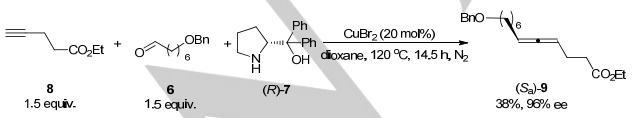
4.2.2.5. Esterification for determination of the ee value of (*R*)-traumatic lactone: synthesis of (*R*)-**13** (zj-8-121)



Typical Procedure VIII: To a Schlenk tube were added (R_a)-traumatic lactone (0.0682 g, 0.3 mmol), DMF (5 mL), K_2CO_3 (0.1243 g, 0.9 mmol), and BnBr (42.8 μl, d = 1.44 g/mL, 0.0617 g, 0.36 mmol). After continuous stirring for 19 h at rt, the reaction was complete as monitored by TLC. The mixture was diluted with water (20 mL) and stirred at rt for 10 min and then extracted with ethyl acetate (20 mL × 4). The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. After filtration and evaporation, the residue was purified by chromatography on silica gel [(eluent: petroleum ether (60-90 °C)/ethyl acetate = 5/1 (600 mL) to 3/1 (400 mL)] to afford (*R*)-**13** (0.0917 g, 96%) as an oil: 92% ee (HPLC conditions: Chiralcel AS-H column, *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, λ = 214 nm, t_R (major) = 51.0 min, t_R (minor) = 42.0 min); $[\alpha]_D^{20}$ = +22.2 (*c* = 1.01, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41-7.26 (m, 5H, ArH), 5.11 (s, 2H, $ArCH_2$), 4.47 (quintet, *J* = 7.1 Hz, 1H, OCH), 2.56-2.47 (m, 2H, CH_2), 2.39-2.24 (m, 3H, CH_2 + one proton from CH_2), 1.91-1.51 (m, 5H, CH_2 × 2 + one proton from CH_2), 1.50-1.20 (m, 8H, CH_2 × 4); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.2, 173.5, 136.0, 128.4, 128.0, 80.8, 65.9, 35.4, 34.1, 28.93, 28.88, 28.8, 28.7, 27.8, 25.0, 24.7; IR (neat) ν (cm^{-1}) 3087, 3061, 3033, 2929, 2856, 1771, 1732, 1498, 1456, 1419, 1383, 1351, 1260, 1195, 1180, 1143, 1132, 1076, 1021; MS (70 ev, EI) m/z (%) 319 (M^+ + 1, 22.16), 318 (M^+, 1.53), 211 (100); HRMS calcd for $C_{19}H_{26}O_4$ [M^+]: 318.1831, found: 318.1836.

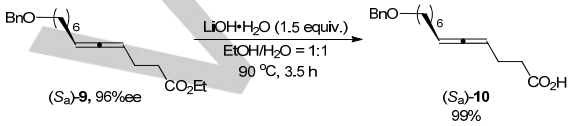
4.2.3. Total synthesis of (*S*)-traumatic lactone

4.2.3.1. Synthesis of ethyl (S_a)-12-(benzyloxy)dodeca-4,5-dienoate (S_a)-**4** (zj-8-112)



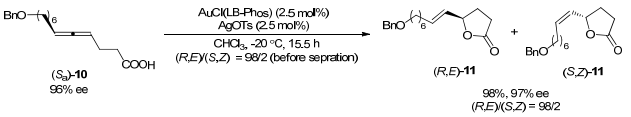
Following **Typical Procedure VI**, the reaction of $CuBr_2$ (0.6759 g, 3.0 mmol, 99%), (*R*)-**7** (3.8781 g, 15 mmol, 98%), **8** (2.8362 g, 22.5 mmol)/dioxane (25 mL), and **6** (4.9559 g, 22.5 mmol)/dioxane (20 mL) for 14.5 h afforded product (S_a)-**9** (1.8805 g, 38%) [(eluent: petroleum ether (60-90 °C)/ethyl acetate = 100/1 (500 mL) to 80/1 (500 mL) to 50/1 (500 mL) to 30/1 (500 mL) to 20/1 (400 mL)] as a liquid: 96% ee (HPLC conditions: Chiralcel AS-H column, *n*-hexane/*i*-PrOH = 100:1, 1.0 mL/min, λ = 214 nm, t_R (major) = 21.2 min, t_R (minor) = 18.4 min); $[\alpha]_D^{20}$ = +49.3 (*c* = 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42-7.18 (m, 5H, ArH), 5.18-5.06 (m, 2H, =CH × 2), 4.49 (s, 2H, $ArCH_2$), 4.12 (q, *J* = 7.1 Hz, 2H, CH_2), 3.46 (t, *J* = 6.8 Hz, 2H, CH_2), 2.45-2.35 (m, 2H, CH_2), 2.34-2.22 (m, 2H, CH_2), 2.01-1.89 (m, 2H, CH_2), 1.67-1.53 (m, 2H, CH_2), 1.47-1.28 (m, 6H, CH_2 × 3), 1.24 (t, *J* = 7.2 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.6, 173.0, 138.6, 128.2, 127.5, 127.4, 92.3, 89.5, 72.8, 70.3, 60.2, 33.4, 29.6, 29.0, 28.9, 28.7, 25.9, 23.8, 14.1; IR (neat) ν (cm^{-1}) 3084, 3063, 3030, 2978, 2931, 2855, 2789, 1962, 1737, 1496, 1454, 1372, 1301, 1251, 1196, 1180, 1158, 1132, 1099, 1076, 1028; MS (70 ev, EI) m/z (%) 331 (M^+ + 1, 11.01), 330 (M^+, 9.50), 91 (100); HRMS calcd for $C_{21}H_{30}O_3$ [M^+]: 330.2195, found: 330.2192.

4.2.3.2. Synthesis of (S_a)-12-(benzyloxy)dodeca-4,5-dienoic acid (S_a)-**10** (zj-8-114)



Following **Typical Procedure III**, the reaction of (S_a)-**9** (1.7107 g, 5.2 mmol), EtOH/H_2O = 1:1 by volume (pre-mixed by using 26 mL of H_2O and 26 mL of EtOH), and LiOH·H_2O (0.3451 g, 7.8 mmol, 95%) for 3.5 h afforded (S_a)-**10** (1.5518 g, 99%) [(eluent: petroleum ether (60-90 °C)/ethyl acetate = 15/1 (300 mL) to 10/1 (550 mL) to 5/1 (600 mL) to 3/1 (400 mL)] as an oil: $[\alpha]_D^{20}$ = +35.8 (c = 0.965, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.05 (bs, 1H, COOH), 7.40-7.21 (m, 5H, ArH), 5.19-5.09 (m, 2H, =CH × 2), 4.51 (s, 2H, $ArCH_2$), 3.46 (t, *J* = 6.6 Hz, 2H, CH_2), 2.50-2.40 (m, 2H, CH_2), 2.35-2.22 (m, 2H, CH_2), 2.02-1.89 (m, 2H, CH_2), 1.68-1.53 (m, 2H, CH_2), 1.46-1.24 (m, 6H, CH_2 × 3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.6, 179.1, 138.5, 128.3, 127.6, 127.4, 92.7, 89.3, 72.7, 70.3, 33.0, 29.5, 28.9, 28.8, 28.6, 25.9, 23.5; IR (neat) ν (cm^{-1}) 3708-2219 (COOH), 1963, 1711, 1496, 1454, 1411, 1362, 1250, 1207, 1160, 1101, 1076, 1028; MS (70 ev, EI) m/z (%) 303 (M^+ + 1, 12.67), 302 (M^+, 3.15), 91 (100); HRMS calcd for $C_{19}H_{26}O_3$ [M^+]: 302.1882, found: 302.1884.

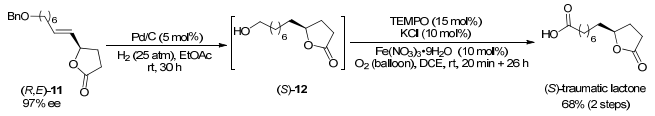
4.2.3.3. Synthesis of (*R*,*E*)-5-(8-(benzyloxy)oct-1-en-1-yl)dihydro-2(3*H*)-furanone (*R*,*E*)-**11** (zj-8-123)



Following **Typical Procedure VII**, the reaction of AgOTs (0.0319 g, 0.1125 mmol, 98%), Au(LB-Phos)Cl (0.0672 g, 0.1125 mmol), $CHCl_3$ (25 mL), and (S_a)-**10** (1.3588 g, 4.5 mmol)/$CHCl_3$ (20 mL) for 15.5 h afforded (*R*,*E*)-**11** (1.3266 g, 98%, (*R*,*E*)/(*S*,*Z*) = 98/2 determined by ^{1}H NMR) [eluent: petroleum ether (60-90 °C)/ethyl acetate = 15/1 (450 mL) to 10/1 (500 mL) to 7/1 (880 mL)] ((*R*,*E*)/(*S*,*Z*) = 98/2 determined by ^{1}H NMR of crude product) as an oil: 97% ee (HPLC conditions: Chiralcel PA-2 column, *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, λ = 214 nm, t_R (major) = 50.9 min, t_R (minor) = 44.1 min; $[\alpha]_D^{20}$ = -21.4 (*c* = 0.98, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40-7.21 (m, 5H, ArH), 5.78 (dtd, J_1 = 15.3 Hz, J_2 = 6.8 Hz, J_3 = 0.8 Hz, 1H, =CH), 5.47 (ddt, J_1 = 15.3 Hz, J_2 = 7.2 Hz, J_3 = 1.4 Hz, 1H, =CH), 4.86 (q, *J* = 7.2 Hz, 1H, CH), 4.49 (s, 2H, CH_2), 3.46 (t, *J* = 6.5 Hz, 2H, CH_2), 2.57-2.44 (m, 2H, CH_2), 2.39-2.26 (m, 1H, one proton from CH_2), 2.05 (q, *J* = 6.7 Hz, 2H, CH_2), 2.01-1.85 (m, 1H, one proton from CH_2), 1.66-1.55 (m, 2H, CH_2), 1.45-1.23 (m, 6H, CH_2 × 3);

the following signals are discernible for (*S*,*Z*)-**11**: δ 5.69-5.59 (m, 1H, =CH), 5.26-5.17 (m, 1H, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.9, 138.5, 135.3, 128.1, 127.4, 127.30, 127.28, 80.9, 72.6, 70.2, 31.8, 29.5, 28.7, 28.6, 28.52, 25.50, 25.8; IR (neat) ν (cm^{-1}) 3088, 3062, 3029, 2927, 2854, 2790, 1771, 1673, 1496, 1455, 1422, 1362, 1327, 1196, 1180, 1142, 1132, 1076, 1009; GC-MS (70 ev, EI) *m/z* (%) for (*R*,*E*)-**11**: t_R (major) = 9.12 min: 302 (M^+, 0.07), 193 [(M - $C_7H_9O)^+$, 7.58], 91 (100); for (*S*,*Z*)-**11**: t_R (minor) = 8.95 min: 193 [(M - $C_7H_9O)^+$, 7.35], 91 (100); Elemental analysis calcd (%) for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67; Found: C, 75.10; H, 8.57.

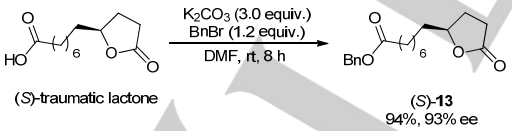
4.2.3.4. Synthesis of (*S*)-traumatic lactone (zj-8-124, zj-8-132)



Following **Typical Procedure V**, the reaction of (*R*,*E*)-**11** ((*R*,*E*)/(*S*,*Z*) = 98/2) (1.2082 g, 4 mmol)/EtOAc (24 mL) and Pd/C (10% on C, dry, 0.2128 g, 0.2 mmol) for 30 h afforded crude (*S*)-**12** (96% NMR yield, determined by ^{1}H NMR of crude product using 1,3,5-trimethylbenzene as internal standard), which was then submitted to next step without further characterization.

Following **Typical Procedure I**, the reaction of $Fe(NO_3)_3{\cdot}9H_2O$ (0.1648 g, 0.4 mmol, 98%), KCl (0.0299 g, 0.4 mmol), TEMPO (0.0956 g, 0.6 mmol, 98%), DCE (10 mL) and (*S*)-**12** (prepared above)/DCE (12 mL) for 26 h afforded (*S*)-traumatic lactone (0.6231 g, 68%, 2 steps) [eluent: petroleum ether (60-90 °C)/ethyl acetate = 5/1 (600 mL) to 3/1 (600 mL) to 2/1 (600 mL) to 1/1 (400 mL)] as a white solid: m. p. 62.9-64.3 °C (*n*-hexane/dichloromethane); $[\alpha]_D^{20}$ = -31.7 (*c* = 1.04, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.25 (bs, 1H, COOH), 4.50 (quintet, *J* = 6.8 Hz, 1H, OCH), 2.55 (dd, J_1 = 9.6 Hz, J_2 = 6.9 Hz, 2H, CH_2), 2.42-2.27 (m, 3H, CH_2 + one proton from CH_2), 1.94-1.53 (m, 5H, CH_2 × 2 + one proton from CH_2), 1.52-1.20 (m, 8H, CH_2 × 4); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.5, 177.5, 80.9, 35.2, 33.7, 28.8, 28.7, 28.60, 28.55, 27.7, 24.8, 24.3; IR (neat) ν (cm^{-1}) 3729-2228 (COOH), 1770, 1709, 1462, 1418, 1356, 1284, 1192, 1180, 1143, 1132, 1076, 1019; MS (70 ev, EI) *m/z* (%) 229 (M^+ + 1, 54.05), 228 (M^+, 2.19), 211 (100), 85 (100); Elemental analysis calcd (%) for $C_{12}H_{20}O_4$: C, 63.14; H, 8.83; Found: C, 63.09; H, 8.67.

4.2.3.5. Esterification for determination of the ee value of (*S*)-traumatic lactone: synthesis of (*S*)-**13** (zj-8-135)

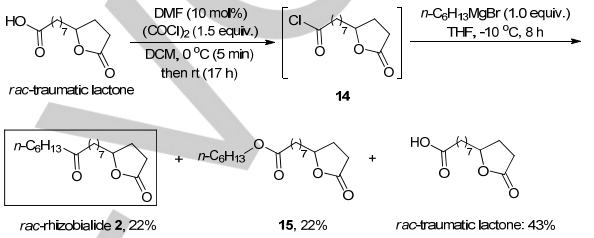


Following **Typical Procedure VIII**, the reaction of (*S*)-traumatic lactone (0.0685 g, 0.3 mmol), DMF (5 mL), K_2CO_3 (0.1243 g, 0.9 mmol), and BnBr (43 uL, d = 1.44 g/mL, 0.0619 g, 0.36 mmol) for 8 h afforded product (*S*)-**13** (0.0894 g, 94%) [(eluent: petroleum ether (60-90 °C)/ethyl acetate = 10/1 (550 mL) to 5/1 (700 mL)] as an oil: 93% ee (HPLC conditions: Chiralcel AS-H column, *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, λ = 214 nm, t_R (major) = 37.6 min, t_R (minor) = 48.5 min); $[\alpha]_D^{20}$ = -22.4 (*c* = 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47-7.24 (m, 5H, ArH), 5.10 (s, 2H, $ArCH_2$), 4.48 (quintet, *J* = 6.8 Hz, 1H, OCH), 2.56-2.45 (m, 2H, CH_2), 2.40-2.21 (m, 3H, CH_2 + one proton from CH_2), 1.90-1.50 (m, 5H, CH_2 × 2 + one proton from CH_2), 1.50-1.19 (m, 8H, CH_2 × 4); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.0, 173.2, 135.8, 128.2, 127.8, 80.7, 65.7, 35.2, 33.9, 28.8, 28.7, 28.6, 28.5, 27.7, 24.8, 24.5; IR (neat) ν (cm^{-1}) 3088, 3064, 3033, 2926, 2855, 1771, 1731, 1498, 1456, 1418, 1384, 1353, 1195, 1180, 1142, 1132, 1076, 1021; MS (70 ev, EI) *m/z* (%) 319 (M^+ + 1, 7.92), 318 (M^+, 1.21), 211 (100); HRMS calcd for $C_{19}H_{26}O_4$ [M^+]: 318.1831, found: 318.1836.

4.3. Synthesis of rhizobialide

4.3.1 Synthesis of *rac*-rhizobialide

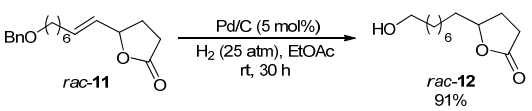
4.3.1.1 Synthesis of *rac*-rhizobialide **2** from *rac*-traumatic lactone **1** (zj-8-125, zj-8-130)



To a flame-dried Schlenk flask were added *rac*-traumatic lactone **1** (114.2 mg, 0.5 mmol), and DCM (1.5 mL) sequentially at rt under nitrogen atmosphere. Then the resulting mixture was cooled by ice-water and DMF (3.9 μl, d = 0.948 g/mL, 3.7 mg, 0.05 mmol) was added. After that, $(COCl)_2$ (63.5 μl, d = 1.5 g/mL, 95.3 mg, 0.75 mmol) was added by syringe within 5 min. Subsequently, the ice-water was removed and the reaction mixture was warmed up to rt gradually and reacted for another 17 h. The resulting mixture was evaporated to give a residue **14**, which was used directly without further purification in the next step.

To another flame-dried Schlenk flask were added *n*-$C_6H_{13}MgBr$ (0.52 mL, c = 1.0 M, 0.52 mmol), and THF (0.5 mL) sequentially at rt under nitrogen atmosphere. The reaction was cooled down to -10 °C and then **14** (prepared above) in THF (1.5 mL) was added within 5min. After being stirred at -10 °C for 8 h, the reaction was quenched with HCl (2 mL, ω = 10%). The flask was removed from the cryogenic reactor and warmed up to rt gradually. The reaction mixture was extracted with DCM (10 mL × 3). The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. After filtration and evaporation, the residue was purified by chromatography on silica gel [eluent: petroleum ether (60-90 °C)/ethyl acetate = 10/1 (550 mL) to 8/1 (450 mL) to 5/1 (600 mL) to 3/1 (480 mL) to 1/1 (600 mL)] on silica gel to afford a mixture of **2** and **15** (66.4 mg, 1:1 (determined by ^{1}H NMR analysis), 22% (**2**), 22% (**15**)), as well as *rac*-traumatic lactone **1** (49.0 mg, 43%).

4.3.1.2 Synthesis of 5-(8-hydroxyoctyl)dihydro-2(3*H*)-furanone *rac*-**12** (zj-8-143)



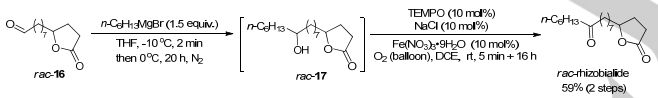
Following **Typical Procedure V**, the reaction of *rac*-**11** (0.4532 g, 1.5 mmol)/EtOAc (9 mL), and Pd/C (10% on C, dry, 0.0799 g, 0.075 mmol)

for 30 h afforded *rac*-**12**[20] (0.2929 g, 91%) [eluent: petroleum ether (60-90 °C)/ethyl acetate = 8/1 (270 mL) to 5/1 (360 mL) to 3/1 (400 mL) to 1.5/1 (500 mL)] as a white solid: m. p. 59.1-60.1 °C (*n*-hexane/dichloromethane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.50 (quintet, J = 6.8 Hz, 1H, OCH), 3.61 (t, J = 6.6 Hz, 2H, OCH_2), 2.54 (dd, J_1 = 9.6 Hz, J_2 = 6.9 Hz, 2H, CH_2), 2.40-2.27 (m, 2H, one proton from CH_2 + OH), 1.93-1.23 (m, 15H, CH_2 × 7 + one proton from CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.4, 81.0, 62.5, 35.3, 32.5, 29.2, 29.1, 29.0, 28.7, 27.8, 25.5, 25.0; IR (neat) ν (cm^{-1}) 3406, 3342, 2988, 2935, 2853, 1755, 1470, 1356, 1234, 1197, 1181, 1127, 1058, 1026, 1009; MS (70 ev, EI) *m/z* (%) 215 (M^+ + 1, 14.09), 214 (M^+, 0.27), 85 (100).

4.3.1.3. Synthesis of 5-(8-oxooctyl)dihydro-2(3*H*)-furanone *rac*-16 (zj-8-148)

Following **Typical Procedure I**, the reaction of $Fe(NO_3)_3{\cdot}9H_2O$ (0.0489 g, 0.12 mmol, 99%), NaCl (0.0071 g, 0.12 mmol), TEMPO (0.0191 g, 0.12 mmol, 98%), DCM (3 mL), and *rac*-**12** (0.2570 g, 1.2 mmol)/DCE (3 mL) at room temperature afforded *rac*-**16**[16a] (0.1848 g, 73%) [eluent: petroleum ether (60-90 °C)/ethyl acetate = 8/1 (360 mL) to 5/1 (600 mL × 2)] as an oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.76 (s, 1H, CHO), 4.50 (quintet, J = 6.8 Hz, 1H, CH), 2.59-2.48 (m, 2H, CH_2), 2.48-2.39 (m, 2H, CH_2), 2.39-2.26 (m, 1H, one proton from CH_2), 1.96-1.53 (m, 5H, CH_2 × 2 + one proton from CH_2), 1.53-1.21 (m, 8H, CH_2 × 4); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.5, 177.0, 80.6, 43.3, 35.0, 28.7, 28.6, 28.5, 28.4, 27.5, 24.7, 21.5; IR (neat) ν (cm^{-1}) 2931, 2857, 2723, 1774, 1723, 1462, 1421, 1390, 1354, 1284, 1219, 1180, 1121, 1018; MS (70 ev, EI) *m/z* (%) 213 (M^+ + 1, 10.52), 212 (M^+, 0.27), 85 (100); HRMS calcd for $C_{12}H_{20}O_3$ [M^+]: 212.1412, found: 212.1416.

4.3.1.4. Synthesis of *rac*-rhizobialide (zj-8-150, zj-8-153)

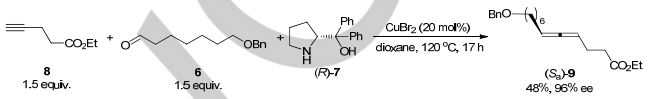


Typical Procedure IX:[21] To a dry Schlenk tube were added *n*-$C_6H_{13}MgBr$ (1.05 mL, 1.05 mmol, 1.0 M in THF), and THF (3 mL) under nitrogen atmosphere. The solution was cooled to -10 °C, and a solution of *rac*-**16** (0.1480 g, 0.7 mmol) in 4 mL of THF was added dropwise at this temperature within 2 min. The resulting mixture was then stirred at 0 °C for 20 h until the reaction was complete as monitored by TLC. The resulting mixture was quenched with a 1.0 M aqueous solution of HCl (1.5 mL) at 0 °C, warmed up to room temperature, and extracted with ethyl acetate (10 mL × 3). The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. After filtration and evaporation, the crude product *rac*-**17** was then used in the next step.

Following **Typical Procedure I**, the reaction of $Fe(NO_3)_3{\cdot}9H_2O$ (0.0286 g, 0.07 mmol, 99%), NaCl (0.0041 g, 0.07 mmol), TEMPO (0.0111 g, 0.07 mmol, 98%), DCE (1.5 mL), and *rac*-**17** (0.7 mmol, prepared above)/DCE (2 mL) at room temperature for 16 h afforded *rac*-rhizobialide (0.1221 g, 59%, 2 steps) [eluent: petroleum ether (60-90 °C)/ethyl acetate = 8/1 (360 mL) to 5/1 (600 mL)] as a white solid: m. p. 56.2-57.3 °C (*n*-hexane/dichloromethane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.49 (quintet, J =6.5 Hz, 1H, OCH), 2.53 (dd, J_1 = 9.2 Hz, J_2 = 7.1 Hz, 2H, CH_2), 2.46-2.24 (m, 5H, CH_2 × 2 + one proton from CH_2), 1.95-1.15 (m, 21H, CH_2 × 10 + one proton from CH_2), 0.88 (t, J = 6.6 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.3, 177.1, 80.8, 42.6, 42.5, 35.4, 31.4, 29.0, 28.92, 28.88, 28.72, 28.65, 27.8, 25.0, 23.6, 23.5, 22.3, 13.8; IR (neat) ν (cm^{-1}) 2953, 2930, 2849, 1778, 1710, 1471, 1462, 1417, 1377, 1265, 1225, 1193, 1127, 1077; MS (70 ev, EI) *m/z* (%) 297 (M^+ + 1, 100); Elemental analysis calcd (%) for $C_{18}H_{32}O_3$: C, 72.93; H, 10.88; Found: C, 72.92; H, 10.60.

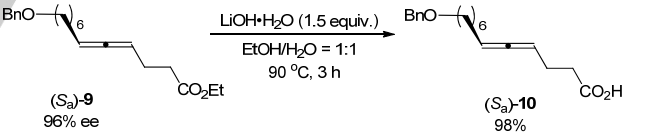
4.3.2. Synthesis of optically active rhizobialide

4.3.2.1. Synthesis of ethyl (S_a)-12-(benzyloxy)dodeca-4,5-dienoate (S_a)-**4** (zj-8-133)



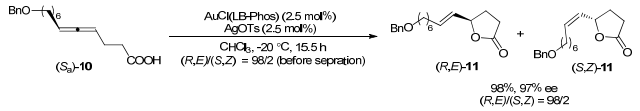
Following **Typical Procedure VI**, the reaction of $CuBr_2$ (0.6759 g, 3.0 mmol, 99%), (*R*)-**7** (3.8711 g, 15 mmol, 98%), **8** (2.8341 g, 22.5 mmol)/dioxane (25 mL), and **6** (4.9505 g, 22.5 mmol)/dioxane (20 mL) for 17 h afforded product (S_a)-**9** (2.3622 g, 48%) [(eluent: petroleum ether (60-90 °C)/ethyl acetate = 100/1 (300 mL) to 50/1 (500 mL × 2) to 30/1 (500 mL) to 20/1 (500 mL) to 10/1 (220 mL)] as a liquid: 96% ee (HPLC conditions: Chiralcel AS-H column, *n*-hexane/*i*-PrOH = 100:1, 1.0 mL/min, λ = 214 nm, t_R (major) = 9.1 min, t_R (minor) = 7.8 min); $[\alpha]_D^{20}$ = +49.4 (c = 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37-7.20 (m, 5H, ArH), 5.18-5.06 (m, 2H, =CH × 2), 4.48 (s, 2H, CH_2), 4.11 (q, J = 7.2 Hz, 2H, CH_2), 3.45 (t, J = 6.6 Hz, 2H, CH_2), 2.44-2.34 (m, 2H, CH_2), 2.33-2.21 (m, 2H, CH_2), 2.02-1.88 (m, 2H, CH_2), 1.68-1.53 (m, 2H, CH_2), 1.47-1.28 (m, 6H, CH_2 × 3), 1.23 (t, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.6, 172.9, 138.6, 128.2, 127.4, 127.3, 92.3, 89.5, 72.7, 70.3, 60.1, 33.3, 29.6, 28.9, 28.8, 28.7, 25.9, 23.8, 14.1.

4.3.2.2. Synthesis of (S_a)-12-(benzyloxy)dodeca-4,5-dienoic acid (S_a)-**10** (zj-8-136)



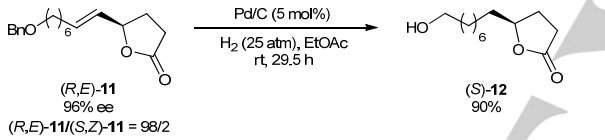
Following **Typical Procedure III**, the reaction of product (S_a)-**9** (2.2454 g, 6.8 mmol), EtOH/H_2O = 1:1 by volume (pre-mixed by using 34 mL of H_2O and 34 mL of EtOH), and $LiOH{\cdot}H_2O$ (0.4510 g, 10.2 mmol, 98%) for 3 h afforded (S_a)-**10** (2.0205 g, 98%) [(eluent: petroleum ether (60-90 °C)/ethyl acetate = 15/1 (300 mL) to 10/1 (550 mL) to 5/1 (300 mL)] as an oil: $[\alpha]_D^{20}$ = +35.7 (c = 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.38 (bs, 1H, COOH), 7.38-7.21 (m, 5H, ArH), 5.20-5.08 (m, 2H, =CH × 2), 4.50 (s, 2H, CH_2), 3.46 (t, J = 6.6 Hz, 2H, CH_2), 2.50-2.39 (m, 2H, CH_2), 2.34-2.22 (m, 2H, CH_2), 2.02-1.89 (m, 2H, CH_2), 1.67-1.54 (m, 2H, CH_2), 1.46-1.24 (m, 6H, CH_2 × 3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.6, 179.1, 138.4, 128.3, 127.6, 127.4, 92.7, 89.3, 72.7, 70.3, 33.0, 29.5, 28.9, 28.8, 28.6, 25.9, 23.4.

4.3.2.3. Synthesis of (*R*,*E*)-5-(8-(benzyloxy)oct-1-en-1-yl)dihydro-2(3*H*)-furanone (*R*,*E*)-**11** (zj-8-137)



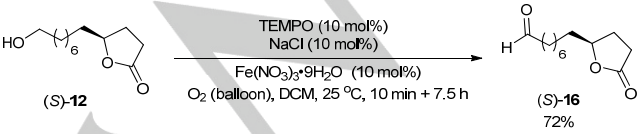
Following **Typical Procedure VII**, the reaction of AgOTs (0.0462 g, 0.1625 mmol, 98%), Au(LB-Phos)Cl (0.0970 g, 0.1625 mmol), $CHCl_3$ (35 mL), and (*S*$_a$)-**10** (1.9627 g, 6.5 mmol)/$CHCl_3$ (20 mL) for 15.5 h afforded (*R*,*E*)-**11** (1.9293 g, 98%, (*R*,*E*)/(*S*,*Z*) = 98/2 determined by ^{1}H NMR) [eluent: petroleum ether (60-90 °C)/ethyl acetate = 15/1 (480 mL) to 10/1 (550 mL) to 7/1 (560 mL × 3)] ((*R*,*E*)/(*S*,*Z*) = 98/2 determined by ^{1}H NMR of crude product) as an oil: 97% ee (HPLC conditions: Chiralcel PA-2 column, *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, λ = 214 nm, t_R (major) = 50.2 min, t_R (minor) = 43.9 min; $[\alpha]_D^{20}$ = -21.0 (*c* = 1.01, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40-7.20 (m, 5H, ArH), 5.78 (dt, J_1 = 15.3 Hz, J_2 = 7.2 Hz, 1H, =CH), 5.47 (dd, J_1 = 15.3 Hz, J_2 = 6.9 Hz, 1H, =CH), 4.85 (q, *J* = 7.1 Hz, 1H, CH), 4.49 (s, 2H, CH_2), 3.46 (t, *J* = 6.8 Hz, 2H, CH_2), 2.49 (dd, J_1 = 9.5 Hz, J_2 = 6.5 Hz, 2H, CH_2), 2.38-2.25 (m, 1H, one proton from CH_2), 2.05 (q, *J* = 6.7 Hz, 2H, CH_2), 2.00-1.85 (m, 1H, one proton from CH_2), 1.66-1.54 (m, 2H, CH_2), 1.44-1.22 (m, 6H, CH_2 × 3); the following signals are discernible for (*S*,*Z*)-**11**: δ 5.67-5.58 (m, 1H, =CH), 5.26-5.16 (m, 1H, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.9, 138.5, 135.2, 128.1, 127.34, 127.28, 127.2, 80.9, 72.6, 70.1, 31.7, 29.4, 28.7, 28.6, 28.5, 25.4, 25.7.

4.3.2.4. Synthesis of (*S*)-5-(8-hydroxyoctyl)dihydro-2(3*H*)-furanone (*S*)-**12** (zj-8-138)



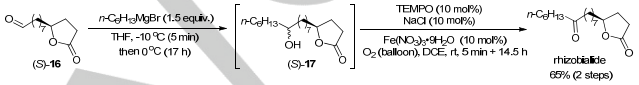
Following **Typical Procedure V**, the reaction of (*R*,*E*)-**11** ((*R*,*E*)/(*S*,*Z*) = 98/2) (1.8116 g, 6 mmol)/EtOAc (30 mL), and Pd/C (10% on C, dry, 0.3190 g, 0.3 mmol) for 29.5 h afforded (*S*)-**12** (1.1505 g, 90%) [eluent: petroleum ether (60-90 °C)/ethyl acetate = 10/1 (330 mL) to 7/1 (350 mL) to 5/1 (600 mL) to 3/1 (600 mL) to 2/1 (600 mL) to 1.5/1 (500 mL) to 1/1 (600 mL)] as a white solid: m. p. 72.1-73.3 °C (*n*-hexane/dichloromethane); $[\alpha]_D^{20}$ = -34.5 (*c* = 0.99, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.50 (quintet, *J* = 6.8 Hz, 1H, CH), 3.62 (t, *J* = 6.6 Hz, 2H, OCH_2), 2.54 (dd, J_1 = 9.2 Hz, J_2 = 7.1 Hz, 2H, CH_2), 2.41-2.26 (m, 1H, one proton from CH_2), 2.15 (s, 1H, OH), 1.94-1.19 (m, 15H, CH_2 × 7 + one proton from CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.4, 81.0, 62.7, 35.4, 32.5, 29.2, 29.10, 29.07, 28.7, 27.8, 25.5, 25.0; IR (neat) ν (cm^{-1}) 3406, 3335, 2986, 2925, 2853, 1755, 1470, 1430, 1356, 1233, 1196, 1181, 1142, 1132, 1076, 1058, 1026, 1009; MS (70 ev, EI) *m/z* (%) 215 (M^+ + 1, 36.12), 214 (M^+, 0.60), 85 (100); Elemental analysis calcd (%) for $C_{12}H_{22}O_3$: C, 67.26; H, 10.35; Found: C, 67.20; H, 10.29.

4.3.2.5. Synthesis of (*R*)-5-(8-oxooctyl)dihydro-2(3*H*)-furanone (*S*)-**16** (zj-8-151)



Following **Typical Procedure I**, the reaction of $Fe(NO_3)_3{\cdot}9H_2O$ (0.1426 g, 0.35 mmol, 98%), NaCl (0.0202 g, 0.35 mmol), TEMPO (0.0558 g, 0.35 mmol, 98%), DCM (8 mL), and (*S*)-**12** (0.7487 g, 3.5 mmol)/DCM (9.5 mL) at room temperature afforded (*S*)-**16** (0.5311 g, 72%) [eluent: petroleum ether (60-90 °C)/ethyl acetate = 8/1 (360 mL) to 6/1 (560 mL) to 4/1 (800 mL)] as an oil: $[\alpha]_D^{20}$ = -34.2 (*c* = 1.02, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.77 (s, 1H, CHO), 4.50 (quintet, *J* = 6.8 Hz, 1H, OCH), 2.58-2.48 (m, 2H, CH_2), 2.48-2.28 (m, 3H, CH_2 + one proton from CH_2), 1.94-1.79 (m, 1H, one proton from CH_2), 1.79-1.53 (m, 4H, CH_2 × 2), 1.52-1.23 (m, 8H, CH_2 × 4); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.5, 177.0, 80.6, 43.4, 35.1, 28.8, 28.7, 28.6, 28.5, 27.6, 24.8, 21.6; IR (neat) ν (cm^{-1}) 2932, 2857, 2722, 1770, 1723, 1462, 1421, 1390, 1353, 1284, 1219, 1180, 1121, 1017; MS (70 ev, EI) *m/z* (%) 213 (M^+ + 1, 56.61), 212 (M^+, 1.43), 85 (100); HRMS calcd for $C_{12}H_{20}O_3$ [M^+]: 212.1412, found: 212.1409.

4.3.2.6. Synthesis of (*S*)-rhizobialide (zj-8-154, zj-8-156)



Following **Typical Procedure IX**, the reaction of *n*-$C_6H_{13}MgBr$ (2.7 mL, 2.7 mmol, 1.0 M in THF), THF (7.5 mL), and (*S*)-**16** (0.3811 g, 1.8 mmol)/THF (10.5 mL) at 0 °C for 17 h afforded the crude product (*S*)-**17**, which was then used in the next step.

Following **Typical Procedure I**, the reaction of $Fe(NO_3)_3{\cdot}9H_2O$ (0.0732 g, 0.18 mmol, 98%), NaCl (0.0104 g, 0. 18 mmol), TEMPO (0.0288 g, 0. 18 mmol, 98%), DCE (3 mL), and (*S*)-**17** (1.8 mmol, prepared above)/DCE (6 mL) at room temperature for 14.5 h afforded (*S*)-rhizobialide (0.3433 g, 65%, 2 steps) [eluent: petroleum ether (60-90 °C)/ethyl acetate = 8/1 (360 mL) to 5/1 (900 mL)] as a white solid: m. p. 61.3-62.6 °C (*n*-hexane/dichloromethane) (Lit.[17] m. p. 54-55 °C); $[\alpha]_D^{20}$ = -24.4 (*c* = 0.54, $CHCl_3$); (Lit.[17] $[\alpha]_D^{26}$ = -19.7 (c = 0.55, $CHCl_3$)); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.49 (quintet, *J* = 6.8 Hz, 1H, OCH), 2.59-2.46 (m, 2H, CH_2), 2.46-2.26 (m, 5H, CH_2 × 2 + one proton from CH_2), 1.95-1.16 (m, 21H, CH_2 × 10 + one proton from CH_2), 0.88 (t, *J* = 6.8 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.8, 176.7, 80.4, 42.2, 42.1, 35.0, 31.1, 28.7, 28.6, 28.5, 28.4, 28.3, 27.5, 24.7, 23.25, 23.17, 22.0, 13.5; IR (neat) ν (cm^{-1}) 2978, 2955, 2931, 2849, 1778, 1710, 1470, 1463, 1419, 1378, 1312, 1226, 1193, 1175, 1128, 1078, 1010; MS (70 ev, EI) *m/z* (%) 298 (M^+ + 2, 100), 297 (M^+ + 1, 100).

Acknowledgements ((optional))

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Keywords: EATA reaction • Gold-catalyzed cyclziation • Asymmetric Total synthesis • Traumatic lactone • Rhizobialide

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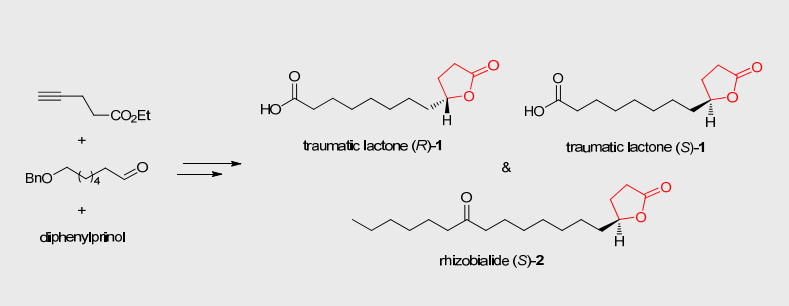

*Jing Zhou, Shihua Song, Chunling Fu, Shengming Ma**

Page No. – Page No.

Efficient Syntheses of Traumatic Lactone and Rhizobialide

The racemic and enantioselective synthesis of Traumatic lactone and Rhizobialide are reported from available starting materials. Excelletnt enantioselectivities were realized by combination EATA reaction with AuCl(LB-Phos)-catalyzed highly stereoselective cycloisomerization.