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Tetrahedron: Asymmetry
Tetrahedron: *Asymmetry* 17 (2006) 2311–2316

Elucidation of the Sharpless epoxidation of zerumbol

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Received 20 June 2006; accepted 21 June 2006
Available online 26 September 2006

Abstract—The Sharpless asymmetric epoxidation of (+)-zerumbol, itself obtained by the reduction of zerumbone **1** gave only all-*erythro* bisepoxide **3** which has five stereogenic centers. Chiral monoepoxide **4**, which decomposed easily under acidic or high-temperature conditions, could also be obtained. The reaction mechanism was revealed to be diastereoselective but non-enantioselective monoepoxidation at the 2,3-position, which proceeded quantitatively followed by a second epoxidation at the 10,11-position, and also proceeded extremely enantioselectively giving an efficient kinetic resolution. Novel asymmetric diepoxydihydroxyzerumbol **6** and triepoxyzerumbol **7** each with seven stereogenic centers were formed with complete diastereoselectivity by dihydroxylation and epoxidation of bisepoxyzerumbol, respectively.

1. Introduction

The concept of diversity oriented synthesis was established by Schreiber in 2000.[1] However, the choice of substrate is important and moreover, if the substrate is a natural material, much chemical development may be needed. Zerumbone **1**,[2] having powerful latent reactivity and containing three double bonds, two conjugated and one isolated, and a double conjugated carbonyl group in an 11-membered ring structure, is a monocyclic sesquiterpene found as the major component of the essential oil of wild ginger, *Zingiber zerumbet* Smith. It is anticipated to be a powerful tool in the implementation of green chemistry with respect to the provision of materials followed on from the cultivation of ginger.

Zerumbone **1** exhibits a variety of interesting reactions, such as transannular ring contraction and cyclization,[3–5] regio- and stereoselective conjugate additions,[3] and various regioselective ring cleavage reactions.[4,6] However, much of its chemistry still remains to be explored in order to fully exploit the ready availability and versatility of this substance as a starting material for conversion to other useful compounds. Not only does zerumbone show attractive reactivity, but zerumbone[7] and its derivatives[6,8] have a broad array of biological activities.

Novel optically active substances as chiral building blocks derived from zerumbone[9,10] can be expected to be of use in a variety of industrial fields such as medicine, perfumery, the liquid crystal industry, and the electronics industry, etc. Moreover, derivatives of zerumbone have potential as non-natural sugar derivatives and to be incorporated into new materials such as a chiral auxiliary.

As shown in Scheme 1, Sharpless asymmetric epoxidation with L-(+)-diethyl tartrate (DET) of racemic zerumbol **2** obtained by reduction of zerumbone gave only the all-*erythro* bisepoxide (−)-(1*R*,2*R*,3*R*,10*S*,11*S*)-**3** which has five stereogenic centers in moderate yield.[9] However, none of the chiral monoepoxy alcohols nor the chiral zerumbols **4** were isolated. Herein, we report the isolation of another chiral product obtained by Sharpless epoxidation of zerumbol and elucidation of the mechanism of this asymmetric epoxidation. Moreover, two novel optically active compounds with seven stereogenic carbons were obtained from bisepoxyzerumbol **3** stereoselectively.

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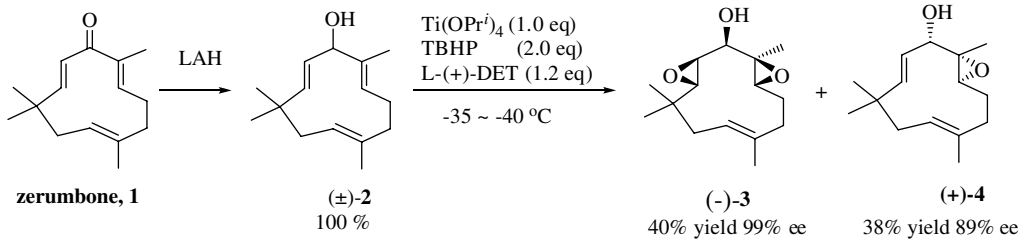
doi:10.1016/j.tetasy.2006.06.049



Scheme 1.

2. Results and discussion

Careful reexamination of the Sharpless asymmetric epoxidation of racemic zerumbol **2** led to the isolation of bisepoxide (−)-**3** (40%) and the monoepoxide (+)-**4** (38%) (Scheme 1). Compound **4**, which decomposed above 40 °C in organic solvents or under weakly acidic conditions was the chiral monoepoxyzerumbol which had a (1*S*,2*S*,3*S*)-configuration. The enantiomeric excess of (+)-**4** was established by GC using a capillary column [CP-CD (CP-cyclodextrin-B-236-M-19), Inj: 200 °C, Det: 200 °C, column: 140 °C, retention time (+)-**4**: 47 min, (−)-**4**: 49 min]. Gaseous **4** did not decompose below 150 °C under GC conditions.

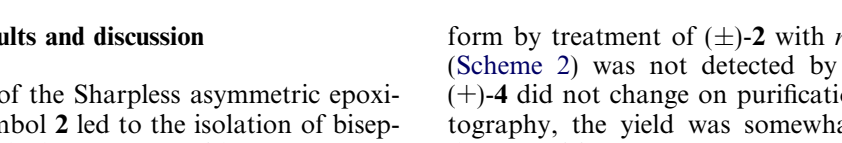
Monitoring the epoxidation of (±)-**2** under a variety of conditions showed that the starting material was completely consumed after 2 h, and suggested that the first formed product was racemic (±)-**4** which was slowly but efficiently kinetically resolved in the second epoxidation step to give (−)-**3**. *threo*-5, which was prepared in racemic form by treatment of (±)-**2** with *m*-chloroperbenzoic acid (Scheme 2) was not detected by TLC. While the ee of (+)-**4** did not change on purification by silica gel chromatography, the yield was somewhat compromised due to decomposition.

As shown in Scheme 3, Sharpless epoxidation of (±)-**2** without DET gave racemic all *erythro*-**3** and **4** in 67% and 28% yield, respectively, without any by-products although racemic *erythro*-**4** was not completely consumed. Moreover, the total yield was very high in the absence of DET. This result suggests that, as expected, the Ti-TBHP system efficiently controls the diastereoselectivity of these reactions.

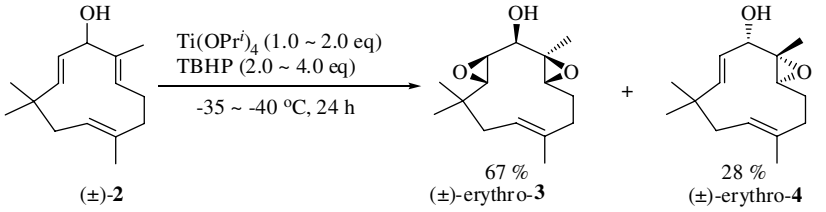
Interestingly, attempted oxidization of (+)-**4** (89% ee) using either L- or D-DET under normal Sharpless reaction conditions failed and no consumption of (+)-**4** was observed even after several hours (Scheme 4). When geraniol (0.5 equiv) was added to the reaction mixture under the same conditions, it was completely epoxidized after 1 h to afford 2,3-epoxygeraniol as confirmed by TLC compared against an authentic sample. This is consistent with (+)-**4** being resistant to epoxidation rather than deactivation of the Sharpless epoxidation catalyst.

Sharpless epoxidation of (±)-**2** with L-DET at −60 °C gave (+)-**4** with a lower ee of approximately 60%.

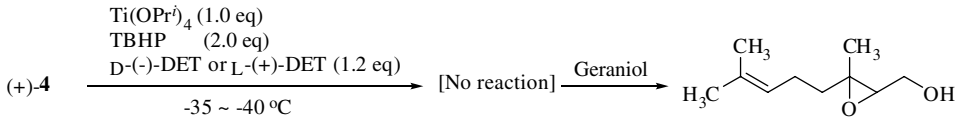
As shown in Scheme 5, (−)-**3** reacted with OsO_4, AD-mixα or AD-mixβ to afford the 6,7-dihydroxy compound (−)-(1*R*,2*R*,3*R*,6*S*,7*S*,10*S*,11*S*)-**6** containing seven stereogenic



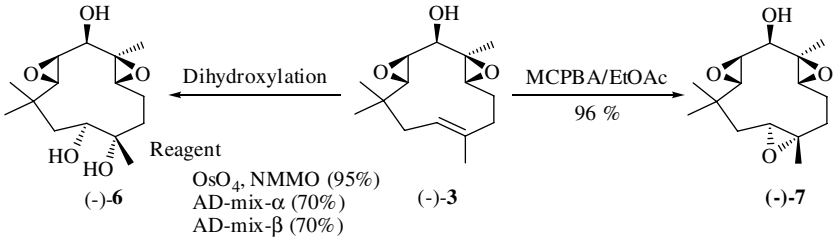
Scheme 2.



Scheme 3.



Scheme 4.



Scheme 5.

centers in over 95% yield. The stereoselectivity of the dihydroxylation of **3** depends on the configuration of the substrate rather than on the chiral catalyst. Moreover, (−)-**3** reacted with MCPBA in ethyl acetate to afford the novel chiral triepoxide (−)-(1*R*,2*R*,3*R*,6*S*,7*S*,10*S*,11*S*)-**7** in 96% yield also with seven stereogenic centers.

2.1. Absolute configuration

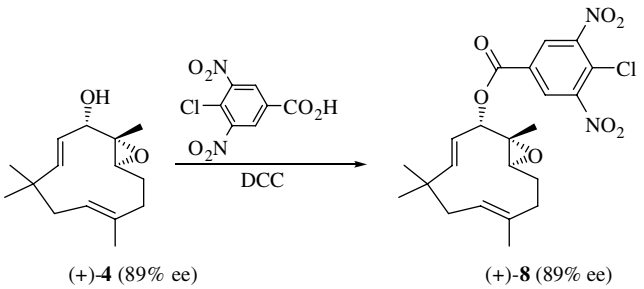
The relative configuration within (+)-**4** was determined by anomalous dispersion of a heavy atom derivative. For this purpose, (+)-**4** (89%) was converted to the 4-chloro-3,5-dinitrobenzoate derivative (+)-**8** (89% ee) (Scheme 6).

Recrystallization of (+)-**8** from EtOH gave triclinic crystals of racemic (±)-(1*SR*,2*SR*,3*SR*)-**8**, one of which was subjected to X-ray analysis (Fig. 1). The absolute configuration of (−)-**3** was assigned as (1*R*,2*R*,3*R*,10*S*,11*S*) on the assumption that the usual selectivity observed in the second Sharpless asymmetric epoxidation with L-DET was operating. From this, the absolute configuration of (+)-**4** was assigned as (1*S*,2*S*,3*S*).

The relative configurations within (1*R*,2*R*,3*R*,6*S*,7*S*,10*S*,11*S*)-**6** and (1*R*,2*R*,3*R*,6*S*,7*S*,10*S*,11*S*)-**7** were also determined by X-ray analysis. Monoclinic crystals were obtained by recrystallization of each from hexane and ethyl acetate (Figs. 2 and 3). The absolute configurations were assigned from that of (−)-**3** from which they were derived.

3. Conclusion

The Sharpless asymmetric epoxidation (with L-DET) of racemic zerumbol (±)-**2** gave racemic *erythro*-2,3-epoxide (±)-**4** regioselectively but not enantioselectively. A second



Scheme 6.

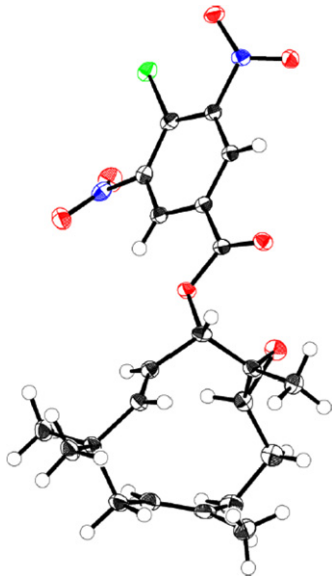


Figure 1. ORTEP drawing of the crystal structure of diepoxy esters (±)-**8**.

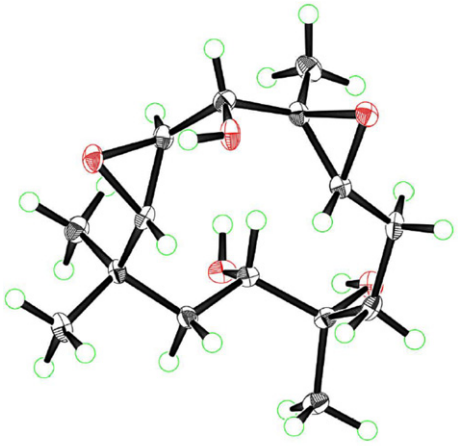


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Figure 2. ORTEP drawing of (−)-**6**.

in situ epoxidation step led to the efficient kinetic resolution of (±)-**4** to generate (−)-**3** on 99% ee. Further diastereoselective oxidation of (−)-**3** led to the formation of (−)-**6** and (−)-**7**, each with seven stereogenic centers.

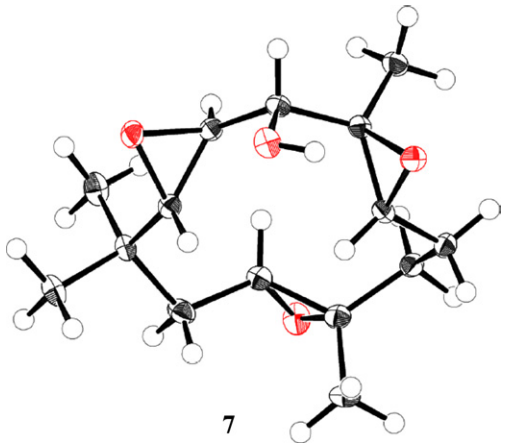

Figure 3. ORTEP drawing of (−)-**7**.

4. Experimental

4.1. General methods

NMR spectra were obtained at 270 MHz for protons and 68 MHz for ^{13}C in $CDCl_3$ with tetramethylsilane (TMS) as the internal standard unless otherwise noted. Chemical shifts δ were reported in parts per million from TMS. Mass spectra were recorded at 70 eV, and high-resolution mass spectra (HRMS) were obtained by direct injection. The X-ray diffraction and CCDC numbers appear in the sections on compound data. Chemicals were of commercially available reagent grade and used without further purification.

4.2. (1*R*,2*R*,3*R*,10*S*,11*S*)-2,3-10,11-Diepoxy-2,6,9,9-tetramethyl-6-cycloundecen-1-ol, (−)-3 and (1*S*,2*S*,3*S*)-2,3-epoxy-2,6,9,9-tetramethyl-6,10-cycloundecadien-1-ol, (+)-4

A mixture of $Ti(OPr^i)_4$ (644 mg, 2.27 mmol) and L-DET (560 mg, 2.72 mmol) in dry CH_2Cl_2 (20 mL) was stirred at −30 °C for 10 min before the addition of **2** (500 mg, 2.27 mmol) and finally 5 M TBHP (0.92 mL, 4.60 mmol). The homogeneous solution was stored in a freezer at −26 °C in a reaction vessel with a septum cap. The progress of the oxidation was monitored by TLC. After 48 h, the flask was placed in a −30 °C bath and 10% aqueous tartaric acid (11.5 mL) was added to the solution with stirring. After 10 min, the cooling bath was removed and stirring continued until the aqueous layer became clear after which the aqueous solution was immediately extracted with CH_2Cl_2 (3 × 30 mL). The combined organic extracts were washed with water (30 mL) and brine (3 × 30 mL), dried over Na_2SO_4, and concentrated on a rotary evaporator below 10 °C to leave a colorless oil whose odor indicated contamination by TBHP. The oil was taken up in ether in an ice bath and stirred with 1 M NaOH (6.8 mL) at 0 °C for 30 min. The ether layer was washed with brine (3 × 30 mL), dried over Na_2SO_4, and concentrated on a rotary evaporator below 10 °C to leave a clear oil. Chromatography on silica gel, eluting with a 4:1 mixture of hexane and EtOAc, afforded (−)-**3** and (+)-**4** in 40% (229 mg) and 38% (204 mg) yield, respectively.

4.3. (1*S*,2*S*,3*S*)-2,3-Epoxy-2,6,9,9-tetramethyl-6,10-cycloundecadien-1-ol, (+)-4

$[\alpha]_D^{23.5} = +19.9$ (*c* 1.16, EtOH) 89% ee, IR (KBr) 3497, 2959, 2927, 1462 cm^{-1}; δ ^1H NMR ($CDCl_3$): δ 1.12 (s, 3H, CH_3 at C9), 1.12 (s, 3H, CH_3 at C9), 1.32 (s, 3H, CH_3 at C6), 1.40–1.49 (m, 1H, H at C4), 1.54 (s, 3H, CH_3 at C2), 1.91–1.95 (m, 2H, H_2 at C8), 2.10–2.26 (m, 3H, H at C4 and 2H at C5), 2.47 (s, 1H, OH at C1), 2.75 (dd, 1H, $J = 3.0$ and 10.6 Hz, H at C3), 4.21 (d, 1H, $J = 4.3$ Hz, H at C1), 4.99 (t, 1H, H at C7), 5.29 (dd, 1H, $J = 4.3$ and 16.2 Hz, H at C11), 5.47 (d, 1H, $J = 16.2$, H at C10); ^{13}C NMR: δ 15.2 (CH_3 at C2), 15.6 (CH_3 at C6), 24.0 (C4), 26.7 (CH_3 at C9), 27.7 (CH_3 at C9), 36.3 (C9), 36.5 (C5), 40.1 (C8), 58.2 (C3), 64.5 (C2), 70.4 (C1), 125.8 (C7), 126.8 (C11), 131.9 (C6), 138.2 (C10). HRMS: *m*/*z* calcd mass for $C_{15}H_{24}O_2$ 236.1776, found 236.1780.

4.4. (1*SR*,2*RS*,3*RS*)-2,3-Epoxy-2,6,9,9-tetramethyl-6,10-cycloundecadien-1-ol, (±)-*threo*-5

A mixture of **2** (300 mg, 1.36 mmol) and MCPBA (259 mg, 1.50 mmol) in ethyl acetate (30 mL) was stirred at 0 °C for 1 h and then at room temperature for 15 h. The progress of the epoxidation was monitored by TLC. Ethyl acetate (10 mL) was added to the reaction mixture and washed with $NaHCO_3$ (5 × 30 mL) and brine (3 × 30 mL), dried over Na_2SO_4, and concentrated on a rotary evaporator. Chromatography on silica gel, eluting with a mixture of EtOAc and hexane (1/3) afforded diastereomerically pure (1*SR*,2*RS*,3*RS*)-**4** in 28% yield. IR (KBr) 3497, 2959, 1462 cm^{-1}; δ ^1H NMR (C_6D_6): δ 0.67 (s, 3H, CH_3 at C9), 0.68 (s, 3H, CH_3 at C9), 0.99 (s, 3H, CH_3 at C6), 0.91–1.03 (m, 1H, H at C4), 1.07 (s, 3H, CH_3 at C2), 1.32–1.82 (m, 5H, H at C4, 2H at C5 and 2H at C8), 2.06 (dd, 1H, $J = 4.3$ and 9.9 Hz, H at C3), 2.73 (s, 1H, OH at C1), 3.38 (d, 1H, $J = 8.6$ Hz, H at C1), 4.53 (dd, 1H, $J = 3.3$ and 10.2 Hz, H at C7), 4.69 (d, 1H, $J = 16.2$ Hz, H at C10), 5.04 (dd, 1H, $J = 8.6$ and 16.2 Hz, H at C11); ^{13}C NMR: δ 11.0 (CH_3 at C2), 14.8 (CH_3 at C6), 24.0 (CH_3 at C9), 25.0 (C4), 29.9 (CH_3 at C9), 36.3 (C9), 36.4 (C5), 40.5 (C8), 60.2 (C3), 66.0 (C2), 81.6 (C1), 125.7 (C7), 126.8 (C11), 132.0 (C6), 141.4 (C10). HRMS: *m*/*z* calcd mass for $C_{15}H_{24}O_2$ 236.1776, found 236.1793.

4.5. (1*R*,2*R*,3*R*,6*S*,7*S*,10*S*,11*S*)-6,7-Dihydroxy-2,3-10,11-bisepoxy-2,6,9,9-tetramethylcycloundecan-1-ol, (−)-6

(i) *OsO_4 method*: A mixture of (−)-bisepoxyzerumbol (120 mg, 0.476 mmol), OsO_4 (242 mg, 0.953 mmol), and *N*-methylmorpholineoxide (NMMO: 562 mg, 4.79 mmol) in acetone/H_2O/CH_3CN (1/1/1, 6 mL) was stirred at 40 °C for 45 h. The progress of the oxidation was monitored by TLC. OsO_4 was removed by filtration and the organic layer concentrated on a rotary evaporator. The aqueous solution was extracted with ethyl acetate (3 × 30 mL). The combined organic extracts were washed with water (30 mL) and brine (3 × 30 mL), dried over Na_2SO_4, and concentrated on a rotary evaporator. Chromatography on silica gel, eluting with EtOAc, afforded enanatiomerically pure (−)-**5** in 95% yield (129.5 mg).

(ii) *AD-mixβ method*: A mixture of AD mix-β (1.40 g), *tert*-BuOH (5 mL), H_2O (5 mL), and $MeSO_2NH_2$ (0.095 g) was cooled to 0 °C, where upon some of the dissolved salts precipitated. Bisepoxyzerumbol, (−)-**3** (0.25 g, 1 mmol) was added and the reaction mixture was stirred with a mechanical stirrer for 24 h at 0 °C, after which time TLC analysis indicated a lack of starting alkene. Sodium sulfite (1.5 g) was added and the mixture stirred for 1 h while it came to room temperature. EtOAc (10 mL) was added and after separation of the layers, the aqueous layer was re-extracted with more EtOAc (3 × 5 mL). The combined extracts were washed with 2 M KOH (15 mL), dried ($MgSO_4$), and the solvent was removed on a rotary evaporator to afford **5** in 70% yield (198 mg). Mp 148–150 °C, $[\alpha]_D^{23.5} = -2.6$ (*c* 1.07, EtOH), IR (KBr) 3481, 2976, 2932, 1479 cm^{-1}; ^1H NMR: δ 0.89 (s, 3H, CH_3 at C6), 1.10 (s, 6H, CH_3 at C9 and CH_3 at C9), 1.26–1.41 (m, 2H, H_2 at C8), 1.45 (s, 3H, CH_3 at C2), 1.63–1.66 (m, 2H, H_2 at C5), 1.87 (d, 2H, $J = 3.9$ Hz, H_2 at C4), 2.35 (s, 1H, OH at C6), 2.54 (s, 1H, OH at C7), 2.72 (dd, 1H, $J = 1.2$ and 15.8 Hz, H at C10), 2.8d, 1H, $J = 3.6$ Hz, H at C3), 3.23 (s, 1H, H at C11), 3.52 (dd, 1H, $J = 3.3$ and 8.6 Hz, H at C1), 4.25 (s, 1H, H at C7); ^{13}C NMR: δ 15.5 (CH_3 at C2), 18.4 (CH_3 at C6), 20.0 (C4), 22.9 (CH_3 at C9), 29.9 (CH_3 at C9), 33.1 (C9), 34.6 (C5), 42.1 (C8), 55.1 (C11), 59.2 (C3 and C10), 62.6 (C2), 66.5 (C7), 70.4 (C1), 74.2 (C6). HRMS: *m*/*z* calcd mass for $C_{15}H_{26}O_5$ 286.1780, found 268.1793.

4.6. X-ray crystallographic study of (−)-6

A colorless prism crystal, crystal size $0.20 \times 0.10 \times 0.10$ mm^3, monoclinic, space group *Cc* (no. 9), $a = 16.73(2)$, $b = 8.518(10)$, $c = 11.051(12)$ Å, $\beta = 105.004(13)°$, $V = 1520.8(30)$ $Å^3$, $Z = 4$, $D_{calcd} = 1.251$ g/cm^3, μ(Mo-Kα) = 0.92 cm^{-1}, was used for data collection. The intensity data were measured on a Rigaku Mercury CCD detector using Mo-Kα radiation at a temperature of −180 ± 1 °C. The structure was solved by direct methods (SIR97)[11] and expanded using Fourier techniques (DIRDIF99).[12] All calculations were performed using the Crystal Structure crystallographic software package. The final cycle of full-matrix least-squares refinement on F^2 was based on 3017 reflections (all data) and 285 variable parameters and gave $R1 = 0.043$ ($I > 2.0\sigma(I)$) and $wR2 = 0.090$ (all data). The value of the goodness of fit indicator was 1.26 (Summary of Data CCDC 285434).

4.7. (1*R*,2*R*,3*R*,6*S*,7*S*,10*S*,11*S*)-2,3-6,7-10,11-Triepoxy-2,6,9,9-tetramethylcycloundecan-1-ol, (−)-7

A mixture of (−)-bisepoxyzerumbol (300 mg, 1.19 mmol) and MCPBA (247 mg, 1.43 mmol) in ethyl acetate (30 mL) was stirred at 0 °C for 1 h and then at room temperature for 21 h. The progress of the epoxidation was monitored by TLC. Ethyl acetate (10 mL) was added to the reaction mixture and washed with $NaHCO_3$ (5 × 30 mL) and brine (3 × 30 mL), dried over Na_2SO_4, and concentrated on a rotary evaporator. Chromatography on silica gel, eluting with a mixture of EtOAc and hexane (1/1), afforded enantiomerically pure (−)-**7** in 96% yield (307 mg). Mp 107–109 °C, $[\alpha]_D^{25.5} = -4.5$ (*c* 0.101, EtOH), IR (KBr) 3447, 2978, 2959, 2934, 1396 cm^{-1}; ^1H NMR; δ 0.91 (s, 3H, CH_3 at C9), 1.14 (s, 3H, CH_3 at C9), 1.35 (s, 3H, CH_3 at C6), 1.43 (s, 3H, CH_3 at C2), 1.60 (s, 2H, H_2 at C4), 1.66 (s, 2H, H_2 at C8), 2.22 (s, 1H, H at C5), 2.30 (t, 1H, $J = 5.3$ Hz, H at C5), 2.60 (d, 1H, $J = 2.6$ Hz, H at C7), 2.88 (s, 1H, H at C10), 2.98 (dd, 1H, $J = 5.3$ and 10.6 Hz, H at C3), 3.11 (s, 1H, H at C11), 4.19 (s, 1H, H at C10) ^{13}C NMR; 15.5 (CH_3 at C2), 16.7 (CH_3 at C6), 18.0 (CH_3 at C9), 25.1 (C4), 29.2 (CH_3 at C9), 33.1 (C9), 35.0 (C5), 37.8 (C8), 55.4 (C3), 55.5 (C11), 58.8 (C10), 60.1 (C6), 60.3 (C2), 61.6 (C7), 68.0 (C1). HRMS: *m*/*z* calcd mass for $C_{15}H_{24}O_4$ 268.1675, found 268.1684.

4.8. X-ray crystallographic study of (−)-7

A colorless prism crystal, crystal size $0.40 \times 0.50 \times 0.18$ mm^3, monoclinic, space group $P2_1$ (no. 4), $a = 9.301(8)$, $b = 5.724(5)$, $c = 13.932(12)$ Å, $\beta = 104.845(9)°$, $V = 716.9(10)$ $Å^3$, $Z = 2$, $D_{calcd} = 1.243$ g/cm^3, μ(Mo-Kα) = 0.88 cm^{-1}, was used for data collection. The intensity data were measured on a Rigaku Mercury CCD detector using Mo-Kα radiation at a temperature of −180 ± 1 °C. The structure was solved by direct methods (SIR97)[11] and expanded using Fourier techniques (DIRDIF99).[12] All calculations were performed using the Crystal Structure crystallographic software package. The final cycle of full-matrix least-squares refinement on F^2 was based on 3164 reflections (all data) and 268 variable parameters and gave $R1 = 0.032$ ($I > 2.0\sigma(I)$) and $wR2 = 0.083$ (all data). The value of the goodness of fit indicator was 1.02 (Summary of Data CCDC 285435).

4.9. (1*SR*,2*SR*,3*SR*)-2,3-Epoxy-2,6,9,9-tetramethyl-6,10-cycloundecadienyl 4-chloro-3,5-dinitrobenzoate, (±)-8

Under an atmosphere of N_2, the mixture of (+)-**4** (40.3 mg, 0.17 mmol), 4-dimethylaminopyridine (4.6 mg, 0.04 mmol), 4-chloro-3,5-dinitrobenzoic acid (43.6 mg, 0.18 mmol), and *N*,*N*′-dicyclohexylcarbodiimide (54.3 mg, 0.26 mmol) in 5 mL anhydrous CH_2Cl_2 was stirred at 0 °C for 5 min and then at room temperature for 3 h. Water (15 mL) was then added to the solution and the reaction stirred for 20 min. The precipitated urea was filtered off and the filtrate extracted with CH_2Cl_2 (2 × 20 mL). The combined organic solutions were washed with 0.5 M HCl and saturated aq $NaHCO_3$, and then dried over Na_2SO_4, and concentrated on a rotary evaporator to afford a colorless solid residue. Chromatography on silica gel, eluting with a 4:1 mixture of hexane and EtOAc afforded **8** in 40% yield. mp 128.0–129.5 °C; IR (KBr) 1278.6, 1349.0, 1549.5, 1731.8 cm^{-1}; ^1H NMR: δ 1.17 (s, 6H, 2 × CH_3 at C9), 1.40 (s, 3H, CH_3 at C2), 1.41–1.49 (m, 1H, H at C4), 1.55 (s, 3H, CH_3 at C6), 1.91 (dd, 1H, $J = 4.4$, 13.9 Hz, H at C8), 1.96–2.03 (m, 1H, H at C4), 2.09 (dd, 1H, $J = 9.9$ and 13.9 Hz, H at C8), 2.22 (m, 2H, H_2 at C5), 2.66 (dd, 1H, $J = 2.9$ and 10.6 Hz, H at C3), 5.11 (dd, 1H, $J = 4.4$, 9.9 Hz, H at C7), 5.42 (dd, 1H, $J = 5.5$ and 16.5 Hz, H at C11), 5.48 (d, 1H, $J = 5.5$ Hz, H at C1), 5.50 (d, 1H, $J = 16.5$ Hz, H at C10), 8.54 (s, 2H, H at C2′); ^{13}C NMR: δ 15.6 (CH_3 at C6), 16.6 (CH_3 at C2), 24.1 (C4), 25.2 (CH_3 at C9), 29.3 (CH_3 at C9), 36.8 (C9), 36.9 (C5), 40.3 (C8), 59.5 (C3), 62.7 (C2), 76.2 (C1),

123.8 (C11), 124.5 (C1′), 124.9 (C7), 128.1 (C2′), 131.0 (C6), 132.8 (C4′), 140.0 (C10), 149.5 (C3′), 160.9 (C=O).

4.10. Crystallographic studies of (±)-8

A colorless prism, $0.60 \times 0.20 \times 0.10$ mm, triclinic, space group $P-1$ (no. 2), $a = 10.158(4)$, $b = 12.081(5)$, $c = 19.656(6)$ Å, $V = 2149.5(13)$ Å^3, $Z = 4$, $D_c = 1.437$ g/cm^3, μ(Mo-Kα) = 2.25 cm^{-1} was used for data collection. The intensity data were measured on a Rigaku RAPID detector using Mo-Kα radiation at a temperature of $-180 + 1$ °C. The structure was solved by direct methods (SIR97)[11] and expanded using Fourier techniques (DIRDIF99).[12] All the calculations were performed using the Crystal Structure crystallographic software package. The final cycle of full-matrix least-squares refinement was based on 9635 observed reflections and 777 variable parameters and gave $R1 = 0.039$ and $wR2 = 0.096$. The value of the goodness of fit indicator was 1.01. (Summary of Data CCDC 611417.)

Acknowledgments

Rhizomes of *Zingiber zerumbet* Smith and zerumbone were supplied by Taiyo Corporation. We wish to express our sincerest gratitude to Professor Tadashi Okamoto for his valuable suggestions and discussions. We thank Dr. Hikaru Takaya for advice and helpful discussions. We are also grateful to Dr. Masanori Morita for the measurement of HRMS. We are indebted to Dr. Masahiro Takatani for his assistance. This work is supported by the Program for Promoting the Advancement of Academic Research at Private Universities, by a grant from Taiyo Corporation, and by SUNBOR Grant from Suntory Institute for Bioorganic Research. This research was partially supported by the Ministry of Education, Science, Sports, and Culture, Grant-in-Aid for Scientific Research (B), 17406003, 2005.

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