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Total Synthesis of (-)-Periplanones C and D. Their Pheromonal Activities against Three *Periplaneta* Species

Yoshinori Nishii, Keisuke Watanabe,[#] Taichi Yoshida, Tatsutoshi Okayama,
Shozo Takahashi,[##] and Yoo Tanabe[*]

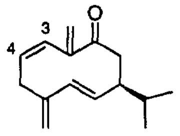
School of Science, Kwansei Gakuin University, 1-1-155 Uegahara, Nishinomiya 662
[#]Agricultural Chemicals Research Laboratory, Sumitomo Chem. Co., Ltd., 4-2-1
Takatsukasa, Takarazuka, Hyogo 665
[##]Pesticide Research Institute, Faculty of Agriculture, Kyoto University, Sakyo-ku, Kyoto 606

Abstract: Total synthesis of (-)-periplanones C [(-)-PC; **1**] and D [(-)-PD; **2**] was achieved starting from (-)-germacrene D *via* 7 and 8 steps, respectively, according to the similar route on syntheses of racemic PC and PD. The ^{1}H NMR and GC mass spectra of **2** unambiguously determined the structure of the natural sample of PD which was isolated from *Periplaneta fuliginosa.* Bioassay of synthetic samples of **1** and **2** was carried out against males of *P. fuliginosa, P. americana,* and *P. japonica.* 10^{-9} g of **1** elicited significant response in males of *P. americana* and *P. japonica.* 10^{-10} g of **2** elicited strong response in *P. fuliginosa* males, whereas it showed significantly weak response against males of *P. americana* and *P. japonica.* Almost same degree of activities was observed between **1** and **2** against males of *P. americana* and *P. japonica* at 10^{-10} g dose. © 1997 Published by Elsevier Science Ltd.

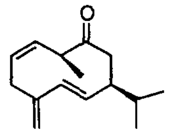
Introduction

Extensive studies on the pheromone chemistry directed toward the insect control have progressed in past few decades.[1] Among these, considerable efforts have been devoted to the investigation for periplanones A-D, sex pheromones of the American cockroach *Periplaneta americana*, and their analogs, whose practical applications to the insect attractant are now drawing attention of many organic and bioorganic chemists. Recently, two authors (Takahashi and Watanabe) have reported the isolation of periplanone D (PD) from Smoky Brown cockroach, *Periplaneta fuliginosa* Serville and its pheromonal activity toward males of *Periplaneta* and *Blatta.*[2]

Hauptmann *et al.* reported that PD was a minor component of *Periplaneta americana* pheromone, which was 100-fold less effective than periplanones A and B.[3] In contrast, PD showed significantly higher activity against *Periplaneta fuliginosa* males, which inhabit wide area in tropical and temperate zones of the world. However, the isolated amount of PD was not enough for the NMR measurements. We planned to obtain sufficient amounts of PD by the synthesis in order to verify the structure and to obtain further information of PD. In line with the rest authors' research for stereostructure-activity relationship of biologically active compounds and their related synthetic studies,[4] we report here a total synthesis of (-)-periplanone C [(-)-PC; **1**] and (-)-PD (**2**), the latter of which corresponds to the first synthesis of its optically active form, and the evaluation of their pheromonal activities against males of *Periplaneta fuliginosa, americana,* and *japonica.*



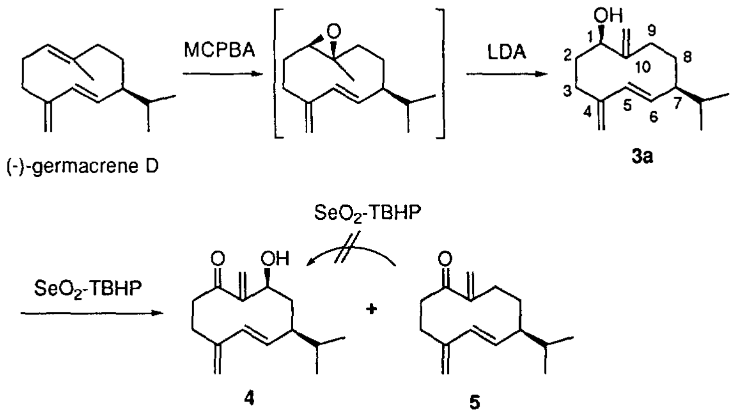
(-)-periplanone C: **1**



(-)-periplanone D: **2**

Results and Discussion

First, the syntheses of (-)-PC (**1**) and its isoster, (-)-PD (**2**) are described. Among hitherto reported synthetic methods, we appreciate combined routes of Shizuri-Yamamura's method for the synthesis (±)-PC[5] and Hauptmann's method for converting (±)-PC into (±)-PD[3] as the promising candidate, because of their brevity (total 8 steps) and accessibility. Moreover, the chiral characteristics depend on the starting optically active (-)-germacrene D, which is much available in natural *ylang ylang* oil.[6] Fortunately, the optical purity of the (-)-germacrene D was very high, 98%ee determined by HPLC analysis.[7] Schemes 1-3 show the synthetic route.

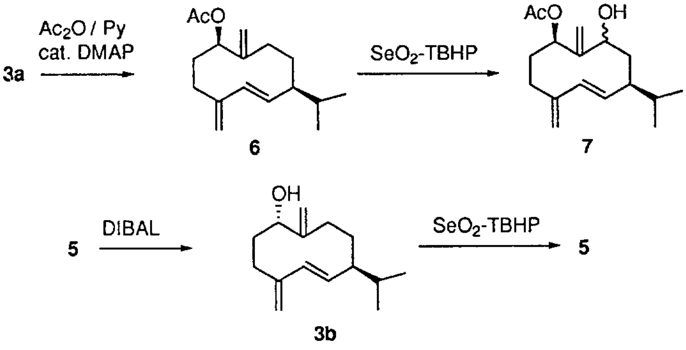


Scheme 1

According to the reported method,[5,7] (-)-germacrene D was converted into 1-hydroxy derivative **3a** ($[\alpha]_D^{18}$ -184.5) through the monoepoxidation, followed by the treatment with LDA. Absolute configuration of **3a** is known as 1*R*, 7*S*.[5a,8] Regioselective allylic oxidation of **3a** by SeO_2/*tert*-butyl hydroperoxide (TBHP), concomitant with oxidizing the parent hydroxyl into carbonyl groups, gave the desired 9-hydroxy derivative **4** (21%; $[\alpha]_D^{18}$ -167.0) together with enone **5** (30%) as a major by-product. The introduction of hydroxyl group in **4** was highly stereoselective. We tried oxidative transformation of **5** into **4** to improve the conversion yield, but this reaction failed to proceed (no reaction) under the identical or several variant conditions. Although the details are not described in the literature,[5a] the whole information clearly indicates that the desirable allylic oxidation of **3a** into **4** and the oxidation of **3a** into **5** occur through absolutely different pathways. Scheme 1 illustrates these results.

To circumvent the undesirable path for giving **5**, the oxidation of protected allyl acetate **6** to allyl alcohol **7** was next examined as shown in scheme 2. The yield was somewhat improved (31%) after optimization of the conditions (0.2 equiv of SeO_2 and 2.0 equiv of TBHP, in THF, 40-45 °C, 3 h). However, we consider that this minor improvement will not compensate for the further tedious transformation toward the target structure, namely, the elimination of AcOH (C3-C4 in **1**), compared with the reported elimination *via* the Bamford-Stevens olefination (*vide infra*).

On the other hand, DIBAL reduction of enone **5** gave the diastereomeric (1*S*, 7*S*)-alcohol **3b** with high stereoselectivity (> 95%) (Scheme 2). This result would be accounted for as following; the hydride of DIBAL attacked the less hindered side of the carbonyl group through the peripheral attack.[9] SeO_2/TBHP oxidation of **3b**, however, did not give the desired 9-hydroxy derivative **4** but resulted just in the formation of enone **5** in 80% yield. It was supposed that SeO_2 could hardly effect the allylic oxidation, because the anchor hydroxyl group of **3b** took a concave site of the germacrene skeleton. Consequently, we turned back to the Shizuri-Yamamura's process (Scheme 3).

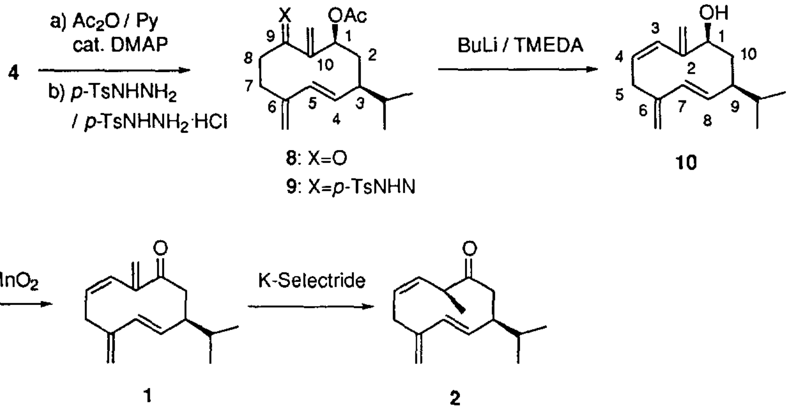


Scheme 2

Acetylation of the 9-hydroxyl group in **4**, followed by the condensation of with *p*-$TsNHNH_2$/*p*-$TsNHNH_2$·HCl gave the corresponding (-)-*p*-tosylhydrazone **9** ($[\alpha]_D^{20}$ -20.0; 53% yield).[10] Several trials of the direct formation of *p*-tosylhydrazone of **4** failed and these reactions gave complex mixtures. The Bamford-Stevens reaction of **9** using BuLi (10 molar amounts) in TMEDA solvent gave alcohol **10** (11%

yield), which was oxidized to (-)-PC (**1**; $[\alpha]_D^{22}$ -264.0) by MnO_2 (43% yield). The optical rotation and the ^1H NMR data were in good accordance with the reported values.[1g]

According to the Hauptmann's procedure using K-Selectride,[5] (-)-PC (**1**) was converted into (-)-PD (**2**; mp 55-57 °C, $[\alpha]_D^{23}$ -329.0). This is the first total synthesis of optically active (-)-PD (**2**). The ^1H NMR and GC mass spectra of the (-)-PD (**2**) unambiguously determined the structure of the natural PD which was isolated from *Periplaneta fuliginosa.*[2]



Scheme 3

Finally, we describe the bioassay results of these synthetic specimens of (-)-PC (**1**) and (-)-PD (**2**) against males of three cockroaches, namely, *P. fuliginosa, P. americana,* and *P. japonica*. Table 1 summarizes these results. It should be noted that (-)-PD (**2**) was remarkably more effective than (-)-PC (**1**) against *P. fuliginosa,* whilst same degree of activities was observed between (-)-PC (**1**) and (-)-PD (**2**) against *P. americana* and *P. japonica.*

In conclusion, we achieved total syntheses of (-)-PC (**1**) and (-)-PD (**2**), and confirmed the unambiguous structure of PD. (-)-PC (**1**) and (-)-PD (**2**) showed high pheromonal activities against males of *P. americana* and *P. japonica.* Against *P. fuliginosa,* however, a clear difference of activities was observed between (-)-PC (**1**) and (-)-PD (**2**), the latter of which had much higher activity. These facts will provide a new and important knowledge to the periplanone chemistry.

Table 1. Pheromone Activities of (-)-PC (**1**) and (-)-PD (**2**).[a]

Species (male)		Dose (g)[b]		
		10^{-11}	10^{-10}	10^{-9}
P. fuliginosa	(-)-PC (**1**)	-	±	+
	(-)-PD (**2**)	++	+++	
P. americana	(-)-PC (**1**)	±	++	+++
	(-)-PD (**2**)	+	++	
P. japonica	(-)-PC (**1**)	-	+	++
	(-)-PD (**2**)	±	+	

a) Detailed procedures and conditions are described in the experimental section.
b) (±): 1 to 3 males responding within 1 min. (+): less than 10 males responding within 1 min. (++): more than 10 males responding within 30 sec. (+++): 30 or more males responding immediately.

Experimental

Melting points were determined on a hot stage microscope apparatus (Yanagimoto) and are uncorrected. ^{1}H NMR spectra were recorded on a JEOL α (400 MHz) spectrometer using a TMS internal standard. ^{13}C NMR spectra (100 MHz) were recorded on a JEOL α (400 MHz) spectrometer using a TMS internal standard. IR spectra were recorded on a JASCO FT/IR-8000 spectrophotometer. MS spectra were obtained with a HP-5971 mass spectrometer coupled with GC Model HP-5890 instruments. HRMS spectra were obtained with a M-003 spectrometer. All reagents and solvents were purified prior to use. Silica-gel column chromatography was performed on a Merck Art. 7734 and 9385. (-)-Germacrene D (ca. 10% content) in *ylang ylang* oil was purified up to ca. 60% by the reported procedure.[7] Compounds **3a**, **4**, and **5** were prepared according to the reported method.[5a,7]

(1*S*,5*E*,7*S*)-7-Isopropyl-4,10-bis(methylene)-5-cyclodecen-1-ol (3b). DIBAL (1.0 M in hexane; 19.8 ml) was added to a stirred solution of ketone **5**[7] (3.83 g, 18 mmol) in hexane/benzene (=1:2; 54 ml) at 0-5 °C and the mixture was stirred for 1.5 h at room temp. The mixture was poured into ice and aqueous sat. NH_4Cl, which was extracted with ether. The organic phase was washed with water, brine, dried (Na_2SO_4), and concentrated to give a residue. This was purified by silica-gel chromatography (hexane/EtOAc= 7:1) to give

3.10g of the product **3b** (78%). Colorless oil; $[\alpha]_D^{25}$ -207.8 (*c* 0.21, $CHCl_3$); IR (neat) 3353, 1454, 974, 887 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85 (3H, d, *J* = 6.8 Hz), 0.94 (3H, d, *J* = 6.8 Hz), 1.24-1.34 (1H, m), 1.56-1.70 (2H, m), 1.80-1.99 (4H, m), 2.05-2.16 (1H, m), 2.25-2.42 (3H, m), 4.05 (1H, d, *J* = 10.3 Hz), 4.75 (1H, s), 4.85-4.90 (2H, m), 5.05 (1H, s), 5.48 (1H, dd, *J* = 9.3 Hz and 16.1 Hz), 5.84 (1H, d, *J* = 16.1 Hz). Based on the data of ^1H NMR, **3b** was the other diastereomer of **3a**[5a,7] which was detected < 5%.

SeO_2-TBHP Oxidation of Alcohol 3b. Alcohol **3b** (148 mg, 0.67 mmol) in CH_2Cl_2 (0.45 ml) was added to a stirred suspension of TBHP (70% aqueous solution; 0.17 g, 1.32 mol) and selenium(IV) oxide (15.0 mg, 0.14 mmol) in CH_2Cl_2 (0.90 ml) at 30-35 °C under a nitrogen atmosphere, and then the mixture was stirred at that temp. for 24 h. 10% aqueous KOH was added to the mixture with adjusting pH to ca. 7.0. Dimethyl sulfide (125 mg) and acetic acid (80 mg) were successively added to the mixture at 0-5 °C, and then the mixture was neutralized by 20% aqueous K_2CO_3 (ca. pH 7.0) and extracted with CH_2Cl_2 (10 ml x 2). The combined organic phase was washed with water, brine, dried (Na_2SO_4), and concentrated to give a residue. This was purified by silica-gel chromatography (hexane/EtOAc = 3:1 to 5:2) to give 122 mg of ketone **5** (80%).[5a,7] Colorless oil; $[\alpha]_D^{25}$ -192.0 (*c* 0.25, $CHCl_3$).

(1*R*,5*E*,7S)-7-Isopropyl-4,10-bis(methylene)-5-cyclodecen-1-yl Acetate (6). A mixture of 1-hydroxy diastereomer **3a** (220 mg, 1.0 mmol), 4-(dimethylamino)pyridine (12 mg, 0.1 mmol), and acetic anhydride (204 mg, 2.0 mmol) in pyridine (28.0 ml) was stored at room temp. for 5 h under a nitrogen atmosphere. The mixture was poured into ice and 1M aqueous $NaHCO_3$ (50 ml) and extracted with ether (20 ml x 2). The combined organic phase was successively washed with chilled 1M aqueous HCl, water, aqueous sat. $NaHCO_3$ solution, brine. This ether extract was dried (Na_2SO_4) and concentrated to give a residue. This was purified by silica-gel chromatography (hexane/EtOAc= 7:1) to give 224 mg of acetate **6** (91%). Colorless oil; $[\alpha]_D^{25}$ -110.0 (*c* 0.10, $CHCl_3$); IR (neat, cm^{-1}) 2955, 1738, 1372, 1252, 1017, 974; ^1H NMR ($CDCl_3$) δ 0.82 (3H, d, *J* = 6.8 Hz), 0.90 (3H, d, *J* = 6.8 Hz), 1.44-1.49 (1H, m), 1.58-1.73 (4H, m), 1.78-1.86 (1H, m), 1.97 (3H, s), 2.00-2.11 (1H, m), 2.18-2.24 (1H, m), 2.42-2.51 (2H, m), 4.89 (1H, s), 4.93 (1H, s), 5.05 (1H, dd, *J* = 4.0 Hz and 12.0 Hz), 5.14 (1H, s), 5.36 (1H, s), 5.44 (1H, dd, *J* = 10.0 Hz and 15.6 Hz), 6.10 (1H, d, *J* = 15.6 Hz).

[1*R*,5*E*,7*S*,9(*R*,*S*)]-9-Hydroxy-7-isopropyl-4,10-bis(methylene)-5-cyclodecen-1-yl Acetate (7). Acetate **6** (100 mg, 0.38 mmol) in THF (0.2 ml) was added to a stirred suspension of TBHP (70% aqueous solution; 98 mg, 0.76 mmol) and selenium(IV) oxide (8.0 mg, 0.08 mmol) in THF (0.8 ml) at 40-45 °C under a nitrogen atmosphere, and then the mixture was stirred at that temp. for 3 h. Following a similar work up in the case oxidazing **3b**, 33 mg of the product **7** (31%) was obtained. Colorless oil; $[\alpha]_D^{25}$ -72.4 (*c* 0.15, $CHCl_3$); IR (neat, cm^{-1}) 3445, 1738, 1447, 1242; ^1H NMR ($CDCl_3$) δ 0.82 (3H, d, *J* = 6.8 Hz), 0.91 (3H, d, *J* = 6.8 Hz), 1.20-1.28 (1H, m), 1.44-1.53 (1H, m), 1.86-2.01 (3H, m), 1.99 (3H, s), 2.16-2.27 (2H, m), 2.41-2.48 (1H, m), 2.66 (1H, brs, O<u>H</u>), 3.93 (1H, d, *J* = 10.7 Hz), 4.78 (1H, dd, *J* = 3.6 Hz and 10.7 Hz), 4.88 (1H, s), 4.93 (1H, s), 5.32 (1H, dd, *J* = 10.0 Hz and 16.1 Hz), 5.52 (1H, s), 5.60 (1H, s), 6.01 (1H, d, *J* = 16.1 Hz). Anal. calcd for $C_{17}H_{26}O_3$: C, 73.35; H, 9.41. Found: C, 73.03; H, 9.75.

[1*S*,3*S*,4*E*]-3-Isopropyl-6,10-bis(methylene)-9-oxo-4-cyclodecen-1-yl Acetate (8). According to the similar procedure for preparing acetate **6**, the reaction using 9-hydroxy derivative **4** (2.60 g, 11 mmol) gave 2.9 g of acetate **8** (90%). Colorless oil; $[\alpha]_D^{25}$ -181.6 (*c* 0.5, $CHCl_3$); IR (neat, cm^{-1}) 3450, 1736, 1610. ^1H NMR ($CDCl_3$) δ 0.82 (3H, d, *J* = 7.0 Hz), 0.88 (3H, d, *J* = 7.0 Hz), 1.48-1.54 (1H, m), 1.70-1.83 (1H, m), 1.94-2.19 (2H, m), 2.02 (3H, s), 2.28-2.37 (1H, m), 2.50-2.59 (1H, m), 2.68-2.80 (1H, m), 2.98-3.08 (1H, m), 4.83 (1H, s), 4.92 (1H, s), 5.16 (1H, dd, *J* = 10.1 Hz and 16.0 Hz), 5.60 (1H, dd, *J* = 3.0 Hz and 10.0 Hz), 5.72 (1H, d, *J* = 16.0 Hz), 5.88 (1H, s), 5.96 (1H, s); ^{13}C NMR ($CDCl_3$) δ 19.39, 20.46, 21.24, 31.92, 33.99, 39.70, 40.88, 47.30, 71.04, 113.14, 122.32, 132.85, 136.33, 146.18, 152.27, 169.51, 201.64. Found: *m/z* 276.1751. Calcd for $C_{17}H_{24}O_3$: M, 276.1727.

[1*S*,3*S*,4*E*]-3-Isopropyl-6,10-bis(methylene)-9-(*p*-tosylhydrazino)-4-cyclodecen-1-yl Acetate (9). A mixture of acetate **8** (2.39 g, 8.7 mmol), *p*-tosylhydrazine (3.38 g, 18 mmol), *p*-tosylhydrazine hydrochloride (3.47 g, 16 mmol), and $MgSO_4$ (100 mg) in THF (200 ml) was refluxed under an argon atmosphere for 6 h. The mixture was poured into ice and aqueous sat. $NaHCO_3$ (200 ml) and extracted with ether. The organic phase was washed with water, aqueous sat. $NaHCO_3$, brine, dried (Na_2SO_4), and concentrated to give a residue. This was purified by silica-gel chromatography (hexane/EtOAc= 3.5:1) to give 2.05 g of hydrazone **9** (53%). Colorless crystals; mp 117-118 °C; $[\alpha]_D^{20}$ -20.0 (*c* 0.1, $CHCl_3$); IR (nujol) 3250, 1750, 1615 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.66 (3H, d, *J* = 6.8 Hz), 0.77 (3H, d, *J* = 6.8 Hz), 0.86-0.94 (1H, m), 1.20-1.40 (3H, m), 1.52-1.68 (1H, m), 2.06 (3H, s), 2.28-2.66 (3H, m), 2.48 (3H, s), 4.48 (1H, d, *J* = 16.0 Hz), 4.66 (1H, s), 5.04 (1H, s), 5.08 (1H, dd, *J* = 10.0 Hz and 16.0 Hz), 5.62 (2H, s), 5.66 (1H, s), 7.48 (2H, d, *J* = 8.0 Hz), 7.97 (2H, d, *J* = 8.0 Hz); ^{13}C NMR ($CDCl_3$) δ 19.53, 20.64, 21.44, 21.53, 26.48, 30.13, 31.53, 42.09, 47.88, 72.83, 113.69, 118.70, 128.96, 129.58, 134.90, 135.71, 144.05, 146.81, 148.15, 157.89, 170.02. Anal. calcd for $C_{24}H_{32}N_2O_4S$: C, 64.84; H, 7.25; N, 6.30. Found: C, 64.54; H, 6.96.

[1*S*,3*Z*,7*E*,9*S*]-9-Isopropyl-2,6-bis(methylene)-3,7-cyclodecadien-1-ol (10). BuLi (1.5 M in hexane; 31 ml, 46 mmol) was added to a stirred solution of hydrazone **9** (2.05 g, 4.61 mmol) in *N,N,N',N'*-tetramethylethylenediamine (80 ml) at -60 °C under an argon atmosphere. The mixture was allowed to warm and then kept at room temp. for 10 h. The reaction mixture was poured into water and then extracted with ether. The organic phase was washed with aqueous sat. $CuSO_4$, water, brine, dried (Na_2SO_4), and concentrated to give a residue. This was purified by silica-gel chromatography (hexane/EtOAc= 8:1 and hexane/ether= 3.5:1) to give 109 mg of alcohol **10** (11%). Colorless oil; $[\alpha]_D^{23}$ -129.0 (*c* 0.1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.84 (3H, d, *J* = 4.0 Hz), 0.92 (3H, d, *J* = 4.0 Hz), 1.00-2.50 (5H, m), 2.70-2.83 (1H, m), 3.23-3.36 (1H, m), 3.86-3.90 (1H, m), 4.72 (1H, s), 4.90 (1H, s), 5.05 (1H, s), 5.30 (1H, s), 5.43-5.50 (2H, m), 5.70 (1H, d, *J* = 16.1 Hz), 6.02 (1H, d, *J* = 11.7 Hz); ^{13}C NMR ($CDCl_3$) δ 20.16, 20.53, 31.61, 34.14, 40.79, 47.88, 74.93, 111.43, 114.11, 127.77, 128.63, 131.01, 138.10, 146.56, 151.52. Found: *m/z* 218.1664. Calcd for $C_{15}H_{22}O$: M, 218.1672. The ^1H NMR data accorded with the reported value.[5b]

(3*Z*,7*E*,9*S*)-9-Isopropyl-2,6-bis(methylene)-3,7-cyclodecadien-1-one (1): (-)-PC. A mixture of alcohol **10** (46 mg, 0.21 mmol) and freshly prepared manganese(IV) oxide (420 mg, 4.83 mmol) in benzene (10.0 ml) was refluxed for 3 h under an argon atmosphere. After cooling, the mixture was filtered with Celite and the solvent was evaporated to give a residue. This was purified by silica-gel chromatography (hexane/ether = 22:1) to give 20 mg of (-)-PC **1** (43%). Colorless oil; $[\alpha]_D^{20}$ -264.0 (*c* 0.15, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.88 (3H, d, *J* = 6.7 Hz), 0.94 (3H, d, *J* = 6.7 Hz), 1.59-1.67 (1H, m), 2.03-2.14 (1H, m), 2.44 (1H, dd, *J* = 5.3 Hz and 10.3 Hz), 2.59 (1H, dd, *J* = 6.8 Hz and 12.2 Hz), 3.00 (1H, dd, *J* = 11.1 Hz and 10.3 Hz), 3.40 (1H, dd, *J* = 9.5 Hz and 12.2 Hz), 4.72 (1H, s), 4.92 (1H, s), 5.46 (1H, s), 5.51 (1H, dd, *J* = 10.1 Hz and 16.5 Hz), 5.57 (1H, ddd, *J* = 6.8 Hz, 9.5 Hz, and 12.0 Hz), 5.76 (1H, s), 5.80 (1H, d, *J* = 16.5 Hz), 6.21 (1H, d, *J* = 12.0 Hz); ^{13}C NMR ($CDCl_3$) δ 20.03, 20.17, 32.29, 34.31, 43.48, 49.80, 112.75, 121.46, 128.59, 129.70, 130.36, 136.36, 145.10, 149.37. The ^1H NMR and optical rotation data accorded with the reported value.[1g]

(2*S*,3*Z*,7*E*,9*S*)-9-Isopropyl-2-methyl-6-methylene-3,7-cyclodecadien-1-one (2): (-)-PD. K-Selectride® (0.1 M in THF; 0.69 ml, 0.069 mmol) was added to a stirred solution of (+)-periplanone C (**1**; 10 mg, 0.046 mmol) in dry THF (2.0 ml) was at -60 °C under an argon atmosphere. After 10 min, the mixture was allowed to warm to 0-5 °C during 10 min and then kept at that temp. for 10 min. Water (1.0 ml), aqueous 10% NaOH (1.2 ml), and aqueous 35% H_2O_2 (0.1 ml) were successively added to the mixture, which was stirred for 60 min at rt. Decantation of organic phase using ether (5.0 ml x 3) and evaporation of the solvent gave a residue (9 mg), which was purified by silica-gel chromatography (hexane/ether = 22:1) to give 3.6 mg of (-)-PD **2**

(36%). Colorless crystals; mp 55-57 °C; $[\alpha]_D^{23}$ -329.0 (*c* 0.15, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.89 (3H, d, *J* = 6.8 Hz), 0.91 (3H, d, *J* = 6.8 Hz), 1.12 (3H, d, *J* = 6.9 Hz), 1.64 (1H, m), 2.13 (1H, m), 2.36 (1H, dd, *J* = 5.1 Hz and 10.1 Hz), 2.54 (1H, dd, *J* = 10.1 Hz and 11.6 Hz), 2.61 (1H, dd, *J* = 6.1 Hz and 12.3 Hz), 3.18 (1H, dd, *J* = 9.0 Hz and 12.3 Hz), 3.57 (1H, m), 4.73 (1H, brs), 4.94 (1H, brs), 5.38 (1H, ddd, *J* = 6.1 Hz, 9.0 Hz, and 12.2 Hz), 5.42 (1H, dd, *J* = 9.1 Hz and 12.3 Hz), 5.65 (1H, dd, *J* = 10.5 Hz and 16.1 Hz), 5.88 (1H, d, *J* = 16.1 Hz); ^{13}C NMR ($CDCl_3$) δ 20.05, 20.16, 28.90, 32.32, 36.55, 46.35, 47.12, 49.84, 112.88,127.42, 128.78, 131.00, 131.24, 134.77; MS (70 eV) *m/z* (rel intensity) 218 (M^+; 13), 203 (5), 175 (39), 133 (54), 105 (88), 93 (100). Found: *m/z* 218.1654. Calcd for $C_{15}H_{22}O$: M, 218.1672. The ^1H NMR and MS spectra data accorded with the reported value.[2,3]

Bioassay. According to the reported procedure,[2] after imaginal ecdysis, each about 50 *P. fuliginosa*, *P. americana*, and *P. japonica* males were isolated in a container (34 x 29 x 27 cm) with a shelter at one end. Test samples in hexane were put on a glass plate (2 x 2 cm) and placed in front of the shelter.

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10. The condition of p-TsNHNH$_2$ and catalytic HCl is reported in the literature.[5a] Combined use of p-TsNHNH$_2$ (2.1 molar amounts) and p-TsNHNH$_2$·HCl (1.8 molar amounts) was found to give good result after the optimization in our hands.

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