Synthesis of Pteroenone and Its Stereoisomers, a Defensive Metabolite of the Abducted Antarctic Pteropod *Clione antarctica*

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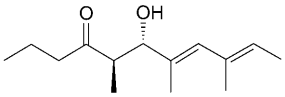
Four stereoisomers of (+)-pteroenone, a defensive metabolite of the abducted Antarctic pteropod *Clione antarctica*, were synthesized by employing *anti*-/*syn*-selective aldol reactions as the key step. These compounds displayed no antifeedant activity against a generally benthic Antarctic fish that does not co-occur with this pteropod.

1. Introduction. – The pteropod *Clione antarctica* is a shell-less, pelagic mollusc which blooms each austral summer in McMurdo Sound, Antarctica. It has an appealing shape, with its mantle adapted as wing-like appendages, and is called a '*sea butterfly*'. It produces a defensive metabolite, called pteroenone, which shows antifeedant activity against its predatory fishes [1][2]. There is a curious commensalism between *C. antarctica* and an Antarctic hyperiid amphipod, *Hyperiella dilatata*, which is a prey of several Antarctic fishes. Predatory fishes do not eat the amphipod grasping a pteropod on its dorsum, due to a feeding deterrent produced by the pteropod [1][2]. *Yoshida et al.* isolated a defensive chemical substance, named pteroenone ((+)-(5*R*,6*S*)-**1**; *Fig.*), and elucidated its configuration [2]. We have synthesized natural (5*R*,6*S*)-**1** and confirmed the absolute configuration [3][4]. In this article, the synthesis of four stereoisomers of **1** and their antifeedant activity against Antarctic fishes are described.



Pteroenone ((+)-(5*R*,6*S*)-**1**)

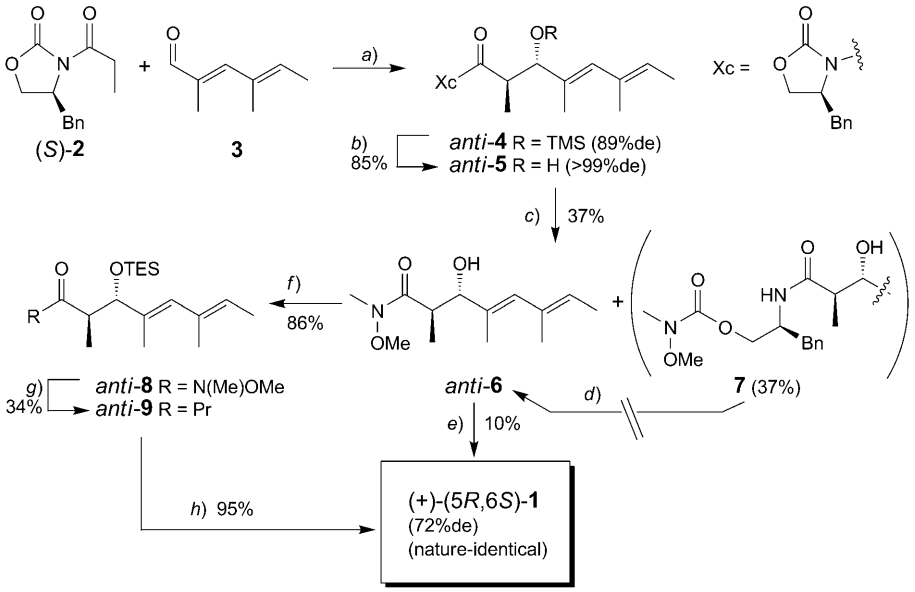
Figure. *Structure of pteroenone*

2. Results and Discussion. – 2.1. *Synthesis of (+)-***1** via *a* Weinreb *Amide.* First, synthesis of natural **1** *via Weinreb* amide was examined. Although pteroenone is a simple molecule, it could be very unstable due to the presence of conjugated diene

system adjacent to *anti*-aldol moiety. Thus, mild reaction conditions and easily removable protecting groups should be used for its synthesis to avoid some unwanted side reactions such as epimerization, *retro*-aldol/aldol reaction, polymerization, dehydration, *etc.*

Scheme 1 depicts our previous synthetic studies reported in [3][4]. The key reaction were *Evans*' *anti*-aldol reaction [5] of (*S*)-**2** [6] with **3** [7], and alkylation *via Weinreb* amides [8], but the yield was low. In addition, the first trial of the deprotection of the Et_3Si (TES) group using HF/Bu_4NF (TBAF) (pH 4) gave (+)-(5*R*,6*S*)-**1** with 72% de (*vide infra*). The details are described in the *Exper. Part*.

Scheme 1. *Synthesis of (+)-(5*R,*6*S*)-**1** via Weinreb *Amides*

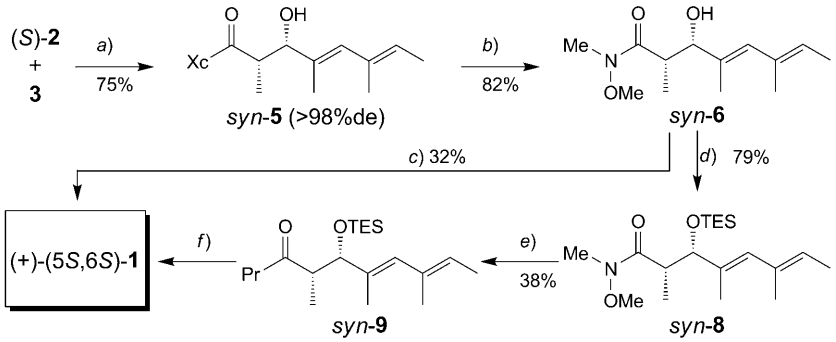


a) $MgCl_2$ (0.2 equiv.), Me_3SiCl (TMSCl; 1.5 equiv.), Et_3N (2 equiv.), AcOEt, r.t., 1 d. *b*) aq. H_2O_2/MeOH; recrystallization. *c*) *d*) Me(MeO)NH·HCl (3 equiv.), $AlMe_3$ (3 equiv.), CH_2Cl_2, −20 to 20°. *e*) PrMgBr (3 equiv.), THF, 0°. *f*) Triethylsilyl trifluoromethanesulfonate (TESOTf; 1.1 equiv.), 2,6-lutidine (1.2 equiv.), CH_2Cl_2, −55°. *g*) PrLi (3 equiv.), THF, −70°. *h*) aq. HF/Bu_4NF (TBAF), THF (pH 4).

2.2. *Synthesis of* syn-*Isomers* via *a* Weinreb *Amide.* We also applied this scheme to the synthesis of the *syn*-isomers (*Scheme 2*). *Evans*' *syn*-aldol reaction [6] afforded pure *syn*-**5** as an oil (>98% de). Transformation of *syn*-**5** to the *Weinreb* amide *syn*-**6** proceeded in 82% yield, and a by-product like **7** was not formed[1]). However, alkylation of *syn*-**6** to (+)-(5*S*,6*S*)-**1** resulted in low yield, and epimerization and *retro*-aldol reaction (to form aldehyde **3**) occurred during the reaction. A similar conversion with

[1]) Conversion of *Evans*' *syn*-aldols to *Weinreb* amides were reported, see [9].

Scheme 2. *Synthesis of (+)-(5S,6S)-***1** via Weinreb *Amide*



a) (*S*)-**2** (1.05 equiv.), Dibutylboron trifluoromethanesulfonate (Bu_2BOTf; 1.15 equiv.), Et_3N (1.2 equiv.), CH_2Cl_2, 0°. *b*) Me(MeO)NH·HCl, $AlMe_3$, THF, −20°. *c*) PrMgBr, THF, −20 to 0°. *d*) Triethylsilyl trifluoromethanesulfonate (TESOTf), 2,6-lutidine, CH_2Cl_2, −30°. *e*) PrLi (2.5 equiv.), THF, −70°. *f*) see *Scheme 4*.

the OH group protected with TES also resulted in low yield (→ *syn*-**8** → *syn*-**9** → (+)-(5*S*,6*S*)-**1**).

2.3. *Synthesis of (+)-***1** *and (−)-***1** via *Thiol Esters*. Since conversion *via* the *Weinreb* amides was troublesome, that of the corresponding thiol esters were examined instead. *Scheme 3* shows the new route to *anti*-isomers. This scheme was described in part in [3][4]. The OH group of *anti*-**5** was protected as its TES ether to give *anti*-**10**. Use of the EE (1-ethoxyethyl) group was also checked but failed in the final step[2]). The chiral auxiliary was reductively removed *via* thio ester *anti*-**11** [10] to afford aldehyde *anti*-**12**[3]). Introduction of the Pr fragment was unexpectedly troublesome. The reaction could be carried out under cryogenic conditions using minimal nucleophile concentrations to avoid the removal of the TES group. As shown in the *Table*, PrLi in Et_2O gave the best result, and the resulting OH group of *anti*-**13** was oxidized to give *anti*-**9**. Removal of the TES group was accomplished using neutral fluoride ion (HF/TBAF) [12] to give (+)-(5*R*,6*S*)-**1** without epimerization (98% ee and 96% de). The overall yield was 47% from **3**. The antipode (−)-*ent*-**1** ((5*S*,6*R*)-**1**; 99% ee and 96% de) was prepared from (*R*)-**2**.

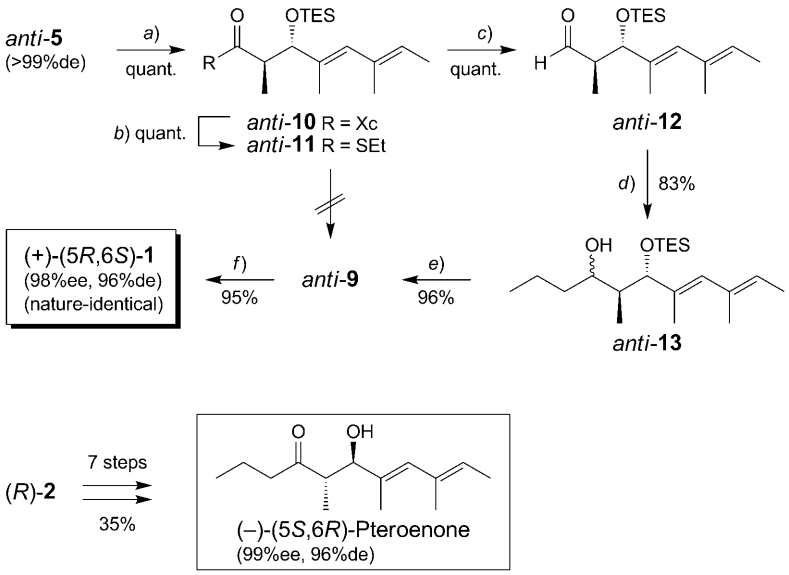
Table. *Alkylation of* **12**

Entry	Conditions	Yield [%]
1	PrMgBr (2.15 equiv.), THF, −15°	42
2	PrLi (6.5 equiv.), THF, −78°	37
3	PrLi (1.1 equiv.), Et_2O, −78°	83
4	PrLi (1.3 equiv.), $CeCl_3$ (1.3 equiv.), THF, −78° [11]	58

[2]) Deprotection of the EE group of the corresponding compound **14** (pyridinium *p*-toluenesulfonate (PPTS), MeOH) gave (+)-**1** with 70% de.

[3]) Direct conversion of thio ester **11** to ketone **14** failed under a variety of *Fukuyama* coupling conditions and organocopper compounds.

Scheme 3. *Synthesis of (+)-(5*R*,6*S*)-***1*** and (−)-(5*S*,6*R*)-***1*** via Thiol Ester*



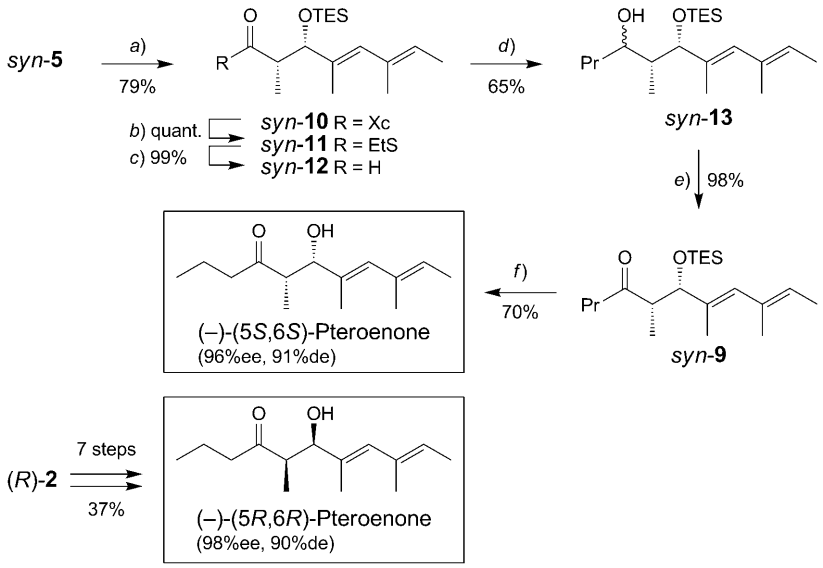
a) TESOTf (1.2 equiv.), 2,6-lutidine (1.2 equiv.), CH_2Cl_2, −55°, 3 h. *b*) EtSH (3.8 equiv.), BuLi (2.6 equiv.), THF, −78 to 7°, 6 h. *c*) Diisobutylaluminum hydride (DIBAL; 1.01 equiv.), CH_2Cl_2, −80°, 20 min. *d*) PrLi (1.1 equiv.), Et_2O, −80°, 30 min. *e*) IBX (4 equiv.), DMSO, r.t., 5 h. *f*) HF/TBAF (pH 7, excess), THF/H_2O, r.t., 2 h.

2.4. *Synthesis of* syn-*Isomers* via *Thiol Esters.* The synthetic pathway to the *syn*-isomers, shown in *Scheme 4*, is similar to that of the *anti*-isomers. The *syn*-epimers of pteroenone were more unstable and partially epimerized during the final purification step (even with the use of neutral SiO_2 for CC), and their diastereoisomeric purities decreased to 90–91% de.

2.5. *Fish Antifeedant Assay.* The synthetic four diastereoisomers of pteroenone showed no antifeedant activity against a benthic fish (*Notothenia coriiceps*) collected near *Palmer* Station, Anvers Island, on the western Antarctic Peninsula. This indicates that fish antifeedant bioactivity is not effective against all fish species, but rather if it does exist in these compounds, it is likely to be targeted against ecologically relevant species of fish such as those that are in sympatry with these pteropods in the Ross Sea, Antarctica.

3. Conclusions. – Four stereoisomers of (+)-pteroenone, a defensive metabolite of the abducted Antarctic pteropod *Clione antarctica*, were synthesized by employing *anti*-/*syn*-selective aldol reactions as the key step. The difference in reactivity and stability between *anti*- and *syn*-aldol compounds was observed. *syn*-Isomers were rather reactive and unstable. These compounds displayed no antifeedant activity against a generally benthic Antarctic fish that does not co-occur with this pteropod, suggesting that if they are deterrent they may be so only against sympatric, ecologically relevant, fish predators.

Scheme 4. *Synthesis of* syn-**1** *Isomers* via *Thiol Ester*



a) TESOTf (1.2 equiv.), 2,6-lutidine (1.2 equiv.), CH_2Cl_2, −55°, 1.25 h. *b*) EtSH (6.9 equiv.), BuLi (4.6 equiv.), THF, −78 to 7°, 6 h. *c*) DIBAL (1.05 equiv.), CH_2Cl_2, −80°, 20 min. *d*) PrLi (2.6 equiv.), Et_2O, −80°, 30 min. *e*) 2-Iodoxybenzoic acid (IBX; 4.0 equiv.), DMSO, r.t., 7 h. *f*) HF/TBAF (pH 7, excess), THF/H_2O, 0°, 0.5 h.

Experimental Part

General. TLC: *Merck* silica gel *60* F_{254} (0.25-mm thickness). Column chromatography (CC): *Merck* silica gel *60* (SiO_2; 70–230 mesh) and *Kanto* silica gel *60N* (70–140 mesh, neutral). HPLC: *Hitachi L-6000* pump and a *Hitachi L-4200 UV-VIS* detector. M.p.: *Yanaco MP-13*; uncorrected. Optical rotations: *Horiba SEPA 300*. IR: *Jasco Report-100*; in cm^{-1}. FT-IR: *Jasco 4100* (ATR); in cm^{-1}. ^{1}H- and ^{13}C-NMR: *Varian Gemini 2000* (300 MHz for ^{1}H and 75 MHz for ^{13}C), *Varian Unity Inova 500* (500 MHz for ^{1}H and 125 MHz for ^{13}C), and *Varian Unity Inova 600* (150 MHz for ^{13}C) rel. to Me_4Si (=0 ppm) in $CDCl_3$ unless otherwise noted; δ in ppm, J in Hz. MS: *Jeol JMS-700*; using 3-nitrobenzyl alcohol (NOBA) as a matrix (FAB); in *m*/*z*. Elemental analysis: *Perkin-Elmer 2400II CHN*.

*(4*S*)-4-Benzyl-3-[(2*R*,3*S*,4*E*,6*E*)-3-hydroxy-2,4,6-trimethylocta-4,6-dienoyl]-1,3-oxazolidin-2-one* (*anti*-**5**). Aldehyde **3** [7] (434 mg, 3.49 mmol) was dissolved in AcOEt (2.8 ml) and added to acyl oxazolidinone (*S*)-**2** [6] (897 mg, 3.84 mmol). The mixture was then treated at r.t. with anh. $MgCl_2$ (66.5 mg, 0.698 mmol), Et_3N (97 µl, 6.99 mmol), and TMSCl (670 ml, 5.24 mmol). After stirring for 24 h, the mixture was filtered through neutral SiO_2 (AcOEt), and the filtrate was concentrated under reduced pressure. The residual oil was dissolved in MeOH (5 ml), treated with CF_3COOH (2 drops) and stirred for 30 min. The mixture was concentrated under reduced pressure. Purification of crude product (89% de) by CC (SiO_2; hexane/AcOEt 6:1 to 5:1) and recrystallization from hexane/AcOEt afforded *anti*-**5** (784 mg, 2.19 mmol, 63%). White needles. M.p. 105–106°. $[\alpha]_D^{24} = +120$ ($c = 0.50$, Et_2O). R_f (hexane/AcOEt 3:1) 0.33. HPLC (column, *Daicel Chiralcel® OD*, 4.6 × 250 mm; temp., 25°; eluent, hexane/i-PrOH 4:1 at 0.5 ml/min; detection at 254 nm): t_R 18.6 (>99% de, >99% ee). IR (KBr): 3450*s* (OH), 2950*m*, 1780*s* (C=O), 1690*s* (C=O), 1400*s*, 1000*s*. ^{1}H-NMR (300 MHz): 7.22–7.37 (*m*, 5 arom. H); 5.92 (*s*, H–C(5′)); 5.45 (*q*, $J = 6.9$, H–C(7′)); 4.66–4.75 (*m*, H–C(4)); 4.11–4.23 (*m*, CH_2(5), H–C(3′), H–C(2′)); 3.33 (*dd*, $J = 13.5$, 3.6, 1 H, PhCH_2); 2.78 (*dd*, $J = 13.5$, 9.6, 1 H, PhCH_2); 2.61 (*d*, $J = 6.3$,

OH); 1.83 (*s*, Me–C(4′)); 1.75 (*s*, Me–C(6′)); 1.69 (*d*, J = 7.2, Me(8′)); 1.09 (*d*, J = 6.3, Me–C(2′)). ^{13}C-NMR (150 MHz): 176.7; 153.8; 135.3; 133.3; 133.0; 132.9; 132.7; 129.5; 128.9; 127.3; 125.3; 125.29; 81.9; 66.0; 55.6; 40.7; 37.7; 16.5; 14.8; 13.7; 12.5. EI-MS: 357 ($M^{+\bullet}$), 339 ($[M-H_2O]^+$), 233, 162, 135, 119, 91. HR-EI-MS: 357.1946 ($M^{+\bullet}$, $C_{21}H_{27}NO_4^+$; calc. 357.1940). Anal. calc. for $C_{21}H_{27}NO_4$: C 70.56, H 7.61, N 3.92; found: C 70.67, H 7.79, N 3.98.

*(−)-(4*R*,2′*S*,3′*R*,4′*E*,6′*E*)-***5*** (*ent-anti-***5**). In the same manner as described for *anti-***5**, **3** (650 mg, 5.23 mmol) was converted to *ent-anti-***5** (1.18 g, 3.30 mmol, 63%). White needles. M.p. 105–106° (hexane/AcOEt). $[\alpha]_D^{24} = -126$ (c = 0.230, Et_2O). HPLC: t_R 16.2 (> 98% de, > 99% ee). HR-FAB-MS: 380.1840 ($[M+Na]^+$, $C_{21}H_{27}NNaO_4^+$; calc. 380.1838). Anal. calc. for $C_{21}H_{27}NO_4$: C 70.56, H 7.61, N 3.92; found: C 70.57, H 7.81, N 3.99.

*(2*R*,3*S*,4*E*,6*E*)-3-Hydroxy-*N*-methoxy-*N*,2,4,6-tetramethylocta-4,6-dienamide* (*anti-***6**) *and (2*S*)-2-{[(2*R*,3*S*,4*E*,6*E*)-3-Hydroxy-2,4,6-trimethylocta-4,6-dienoyl]amino}-3-phenylpropyl Methoxy(methyl)-carbamate* (**7**). To a soln. of MeONHMe · HCl (78 mg, 0.8 mmol) in dry CH_2Cl_2 (0.6 ml) was added a soln. of Me_3Al in hexane (1.0M, 0.8 ml, 0.8 mmol) at 0°, and the mixture was stirred at 20° for 1 h under N_2. The soln. was cooled to −20° before the addition of *anti-***5** (162 mg, 0.40 mmol) in dry CH_2Cl_2 (0.8 ml), and the mixture was stirred at 20° for 12 h. The reaction was quenched with sat. aq. *Rochelle*'s salt soln. and extracted with CH_2Cl_2. The extract was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified with prep. TLC (SiO_2; hexane/AcOEt 2:1) to give *anti-***6** (32 mg, 37%) and **7** (37%).

Data for anti-**6**. White needles. M.p. 58.5–59.5 (i-Pr_2O). $[\alpha]_D^{26} = +6.7$ (c = 0.70, Et_2O). R_f (hexane/AcOEt 4:1) 0.12. FT-IR: 1743*s* (C=O), 1242*m*, 1025*m*, 702*s*. ^{1}H-NMR (300 MHz): 5.90 (*s*, H–C(5)); 5.41 (*qt*, J = 6.4, 1.5, H–C(7)); 4.15 (*pseudo-dd*, J = 7.6, 5.4, H–C(3)); 3.74 (*s*, MeO); 3.21 (*s*, MeN); 3.14–3.22 (*m*, H–C(2)); 2.89 (*d*, J = 5.4, OH); 1.78 (*d*, J = 1.2, Me–C(4)); 1.74 (*s*, Me–C(6)); 1.68 (*d*, J = 6.4, Me(8)); 1.09 (*d*, J = 7.3, Me–C(2)). EI-MS: 241 ($M^{+\bullet}$), 224, 210, 135, 117. HR-EI-MS: 241.1680 ($M^{+\bullet}$, $C_{13}H_{23}NO_3^+$; calc. 241.1678).

Data for **7**. White needles. M.p. 98–99°. FT-IR: 3304*m* (N–H), 1739*m*, 1711*m*, 1644*s* (C=O), 1548*s*, 1164*s*, 1006*s*, 753*s*, 701*s*. ^{1}H-NMR (300 MHz): 7.20–7.36 (*m*, 5 arom. H); 6.18 (*d*, J = 8.5, NH); 5.90 (*s*, H–C(5)); 5.40 (*qt*, J = 6.8, 1.5, H–C(7)); 4.41–4.53 (*m*, $PhCH_2CH$); 4.18 (*dd*, J = 11.3, 6.3, 1 H, CH_2O); 4.13 (*dd*, J = 11.3, 4.1, 1 H, CH_2O); 4.00 (*dd*, J = 7.8, 3.5, H–C(3)); 3.71 (*s*, MeO); 3.16 (*s*, MeN); 2.95 (*dd*, J = 13.7, 6.0, 1 H, $PhCH_2$); 2.82 (*d*, J = 8.0, OH); 2.80 (*dd*, J = 13.7, 8.0, 1 H, $PhCH_2$); 2.37 (*dq*, 7.9, 7.1, H–C(2)); 1.83 (*d*, J = 1.1, Me–C(4)); 1.73 (*s*, Me–C(6)); 1.67 (*d*, J = 6.9, H–C(8)); 1.03 (*d*, J = 7.2, Me–C(2)). FAB-MS: 441 ($[M+Na]^+$), 419 ($[M+H]^+$), 401 ($[M+H-H_2O]^+$). HR-FAB-MS: 419.2547 (M^+, $C_{23}H_{35}N_2O_5^+$; calc. 419.2546).

*(2*R*,3*S*,4*E*,6*E*)-*N*-Methoxy-*N*,2,4,6-tetramethyl-3-[(triethylsilyl)oxy]octa-4,6-dienamide* (*anti-***8**). To a soln. of *anti-***6** (33 mg, 0.14 mmol) in CH_2Cl_2 (0.5 ml) was successively added 2,6-lutidine (0.019 ml, 17 mg, 0.16 mmol) and TESOTf (0.034 ml, 40 mg, 0.15 mmol) at −55°, and the mixture was stirred for 12 h, while the temp. being raised to −15°. Then, the reaction was quenched with H_2O. The aq. layer was extracted with Et_2O, and the combined org. layers were washed with brine, dried ($MgSO_4$), filtered, and concentrated. Purification of the crude product by CC (SiO_2; hexane/AcOEt 6:1) afforded *anti-***8** (41.0 mg, 0.12 mmol, 86%). Colorless oil. $[\alpha]_D^{26} = +16$ (c = 0.045, $CHCl_3$). R_f (hexane/AcOEt 3:1) 0.68. FT-IR: 1664*s* (C=O), 1064*s*, 1007*s*, 743*s*. ^{1}H-NMR (500 MHz): 5.83 (*s*, H–C(5)); 5.39 (*q*, J = 7.0, H–C(7)); 4.16 (*d*, J = 9.5, H–C(3)); 3.75 (*s*, MeO); 3.19 (*s*, MeN); 3.19 (overlapped *m*, H–C(2)); 1.74 (*s*, Me); 1.73 (*s*, Me); 1.69 (*d*, J = 7.0, Me(8)); 0.97, 0.93, 0.89 (3*t*, J = 8.0, $(MeCH_2)_3Si$); 0.87 (*d*, J = 6.5, Me–C(2)); 0.60, 0.53, 0.52 (3*q*, J = 8.0, $(MeCH_2)_3Si$). EI-MS: 355 ($M^{+\bullet}$), 326 ($[M-Et]^+$), 295 ($[M-MeNOMe]^+$), 262, 239 ($[M-MeCHC(=O)N(Me)OMe]^+$), 200, 107, 91, 77. HR-EI-MS: 355, 2544 ($M^{+\bullet}$, $C_{19}H_{37}NO_3Si^+$; calc. 355.2543).

*(5*R*,6*S*,7*E*,9*E*)-5,7,9-Trimethyl-6-[(triethylsilyl)oxy]undeca-7,9-dien-4-one* (*anti-***9**) *from* anti-**8**. To a soln. of *anti-***8** (50 mg, 0.14 mmol) in THF (1 ml) was added PrLi in Et_2O (1.28M, 0.33 ml, 0.42 mmol) at −70°. After stirring for 18 h, the reaction was quenched with sat. aq. NH_4Cl soln., and the mixture was extracted with AcOEt. The org. layers were washed with brine, dried ($MgSO_4$), filtered, and concentrated. Purification of crude product by CC (SiO_2; hexane/AcOEt 15:1) afforded *anti-***9** (16 mg, 0.047 mmol, 34%). Colorless oil. The physical and spectral data: *vide infra*.

(4S)-4-Benzyl-3-[(2R,3S,4E,6E)-2,4,6-trimethyl-3-[(triethylsilyl)oxy]octa-4,6-dienoyl]-1,3-oxazolidin-2-one (*anti*-**10**). A $-55°$ soln. of *anti*-**5** (200 mg, 0.559 mmol) in CH_2Cl_2 (3.5 ml) was treated with 2,6-lutidine (78 µl, 72 mg, 0.67 mmol), followed by TESOTf (151 µl, 0.671mmol). After 80 min, the reaction was quenched by H_2O. The aq. layer was extracted with Et_2O, and the combined org. layers were washed with brine, dried ($MgSO_4$), filtered, and concentrated. Purification of the crude product by CC (SiO_2; hexane/AcOEt 6:1) afforded *anti*-**10** (264 mg, 0.559 mmol, quant.). Colorless oil. R_f (hexane/AcOEt 3:1) 0.53. $[\alpha]_D^{24} = +32$ ($c = 1.2$, Et_2O). IR (film): 2950*m*, 1780*s* (C=O), 1700*s* (C=O), 1380*s*, 1220*s*, 1080*s*, 740*s*. ^{1}H-NMR (300 MHz): 7.25–7.38 (*m*, 5 arom. H); 5.86 (*s*, H–C(5′)); 5.42 (*q*, $J = 6.9$, H–C(7′)); 4.65–4.74 (*m*, H–C(4)); 4.35 (*d*, H–C(3′)) 4.08–4.21 (*m*, CH_2(5), H–C(2′)); 3.39 (*dd*, $J =$ 13.2, 3.3, 1 H, PhCH_2); 2.70 (*dd*, $J = 13.2$, 9.9, 1 H, PhCH_2); 1.78 (*d*, $J = 0.9$, Me–C(4′)); 1.75 (*s*, Me–C(6′)); 1.70 (*d*, $J = 6.9$, Me(8′)); 0.97 (*d*, $J = 7.2$, Me–C(2′)); 0.931 (*t*, $J = 7.8$, (*Me*CH_2)$_3$Si); 0.57 (*q*, $J = 7.8$, (MeCH_2)$_3$Si). ^{13}C-NMR (150 MHz): 176.3; 153.1; 135.6; 134.1; 133.0; 132.8; 129.4; 128.9; 127.2; 124.8; 82.2; 65.6; 55.3; 41.8; 38.0; 22.6; 16.4; 14.6; 13.6; 12.2; 6.89; 6.38; 4.80. EI-MS: 471 ($M^{+\bullet}$), 442 ($[M - Et]^+$), 339 ($[M - TESOH]^+$), 318, 294, 262, 239, 115, 87. HR-EI-MS: 471.2811 ($M^{+\bullet}$, $C_{27}H_{41}NO_4Si^+$; calc. 471.2804).

(4R,2′S,3′R,4′E,6′E)-Isomer (*ent-anti*-**10**). In the same manner as described for *anti*-**10**, *ent-anti*-**5** (633 mg, 1.77 mmol) afforded *ent-anti*-**10** (835 mg, 1.77 mmol, quant.). Colorless oil. $[\alpha]_D^{24} = -29$ ($c =$ 0.18, Et_2O). HR-FAB-MS: 494.2706 ($[M + Na]^+$, $C_{27}H_{41}NNaO_4Si^+$; calc. 494.2702).

S-*Ethyl (2R,3S,4E,6E)-2,4,6-Trimethyl-3-[(triethylsilyl)oxy]octa-4,6-dienethioate* (*anti*-**11**). To a soln. of EtSH (99 µl, 1.3 mmol) in THF (5 ml) was added dropwise BuLi in hexane (1.6M, 0.56 ml, 0.89 mmol) at $-78°$ under Ar, and the mixture was stirred for 25 min. Then, to the mixture was added a soln. of *anti*-**10** (164 mg, 0.35 mmol) in THF (2 ml). The mixture was gradually warmed to 0°, and the reaction was quenched with sat. aq. $NaHCO_3$ soln., and the resulting mixture was extracted with Et_2O. The combined extract was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo*. It was chromatographed on SiO_2. Elution with (hexane/AcOEt 10:1) gave *anti*-**11** (123 mg, 0.35 mmol, quant.). Colorless oil. $[\alpha]_D^{24} = -11$ ($c = 0.36$, Et_2O). R_f (hexane/AcOEt 6:1) 0.67. IR (film): 2950*m*, 2900*s*, 1690*s* (C=O), 1460*s* (C=O), 1240*s*, 1070*s*, 1000*s*, 960*s*, 740*s*. ^{1}H-NMR (300 MHz): 5.80 (*s*, H–C(5)); 5.38 (*q*, $J = 6.6$, H–C(7)); 4.17 (*d*, $J = 9.6$, H–C(3)); 2.87 (*q*, $J = 7.5$, MeCH_2S); 2.81 (*dq*, $J = 9.6, 6.9$, H–C(2)); 1.72 (*s*, Me–C(4)); 1.69 (*s*, Me–C(6)); 1.68 (*d*, $J = 6.6$, Me(8)); 1.25 (*t*, $J = 7.5$, *Me*CH_2S); 0.91 (*d*, $J = 6.9$, Me–C(2)); 0.90 (*t*, $J = 7.8$, (*Me*CH_2)$_3$Si); 0.53 (*q*, $J = 7.8$, (MeCH_2)$_3$Si). ^{13}C-NMR (150 MHz): 202.9; 133.9; 132.8; 132.6; 124.6; 81.7; 53.1; 23.2; 16.4; 15.0; 14.6; 13.6; 11.9; 6.79; 6.38; 4.68. EI-MS: 356 ($M^{+\bullet}$), 327 ($[M - Et]^+$), 239. HR-EI-MS: 356.2202 ($M^{+\bullet}$, $C_{19}H_{36}O_2SSi^+$; calc. 356.2205).

(2S,3R,4E,6E)-Isomer (*ent-anti*-**11**). In the same manner as described for *anti*-**11**, *ent-anti*-**10** (888 mg, 1.88 mmol) afforded *ent-anti*-**11** (638 mg, 1.79 mmol, 95%). Colorless oil. $[\alpha]_D^{24} = +14$ ($c = 1.0$, Et_2O). HR-FAB-MS: 357.2286 ($[M + H]^+$, $C_{19}H_{37}O_2SiS^+$; calc. 357.2284).

(2R,3S,4E,6E)-2,4,6-Trimethyl-3-[(triethylsilyl)oxy]octa-4,6-dienal (*anti*-**12**). A flask was charged with *anti*-**11** (47 mg, 0.1318 mmol) in dry CH_2Cl_2 (0.75 ml) at $-80°$. To the soln. was added DIBAL in hexane (0.94M, 266 µl, 0.283 mmol). After 50 min, the mixture was stirred with aq. *Rochelle* salt soln., then extracted with Et_2O. The combined extract was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo* to give *anti*-**12** in an almost quant. yield. Colorless oil. $[\alpha]_D^{24} = +10$ ($c = 1.95$, Et_2O). R_f (hexane/AcOEt 6:1) 0.43. IR (film): 2950*m*, 2855*s*, 1725*s* (C=O), 1060*s*. ^{1}H-NMR (300 MHz): 9.78 (*d*, $J = 2.7$, H–C(1)); 5.82 (*s*, H–C(5)); 5.40 (*q*, $J = 6.9$, H–C(7)); 4.08 (*d*, $J = 8.7$, H–C(3)); 2.54–2.65 (*m*, H–C(2)); 1.73 (*s*, Me–C(4)); 1.70 (*s*, Me–C(6)); 1.68 (*d*, $J = 6.9$, Me(8)); 0.90 (*t*, $J = 8.4$, (*Me*CH_2)$_3$Si); 0.88 (*d*, $J = 6.9$, Me–C(2)); 0.57 (*q*, $J = 8.4$, (MeCH_2)$_3$Si). ^{13}C-NMR (150 MHz): 205.5; 133.6; 132.7; 132.3; 124.9; 80.9; 50.2; 23.0; 16.4; 13.7; 12.4; 11.0; 6.79; 4.76. EI-MS: 296 ($M^{+\bullet}$), 267 ($[M -$ Et]$^+$), 239, 217, 115 ($[Et_3Si]^+$), 87. HR-EI-MS: 296.2174 ($M^{+\bullet}$, $C_{17}H_{32}O_2Si^+$; calc. 296.2172).

(4RS,5R,6S,7E,9E)-5,7,9-Trimethyl-6-[(triethylsilyl)oxy]undeca-7,9-dien-4-ol (*anti*-**13**). To a soln. of *anti*-**12** (22 mg, 0.0742 mmol) in Et_2O (0.5 ml) was added PrLi in Et_2O (1.3M, 63 µl, 0.0816 mmol) at $-80°$ under Ar, and the mixture was stirred for 30 min. The reaction was quenched with sat. aq. NH_4Cl soln., and the resulting mixture was extracted with Et_2O. The combined extract was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo*. Purification of the crude product by TLC (hexane/AcOEt 15:1) afforded *anti*-**13** (21 mg, 0.062 mmol, 83%). Colorless oil. R_f (hexane/AcOEt 6:1) 0.52. IR (film): 3450*s* (br., OH), 2900*s*, 1450*s*, 1050*s*. ^{1}H-NMR (300 MHz): 5.91 (*s*, H–C(8)); 5.36 (*q*, $J = 6.6$, H–C(10));

4.04 (*d*, *J* = 5.1, H–C(6)); 3.84–3.92 (*m*, H–C(4)); 3.13 (*d*, *J* = 3.6, OH); 1.73 (*s*, Me–C(7)); 1.69 (*d*, *J* = 6.0, Me(11)); 1.68 (*s*, Me–C(9)); 1.43–1.52 (*m*, CH_2(3), H–C(5)); 1.24–1.34 (*m*, CH_2(2)); 0.96 (*t*, *J* = 7.2, (*Me*CH_2)$_3$Si); 0.92 (*t*, *J* = 6.9, Me(1)); 0.88 (*d*, *J* = 7.2, Me–C(5)); 0.62 (*q*, *J* = 7.2, (MeC*H*$_2$)$_3$Si). ^{13}C-NMR (150 MHz): 134.4; 133.0; 130.3; 124.0; 82.9; 71.0; 65.8; 39.3; 36.3; 19.5; 16.6; 15.3; 14.4; 14.1; 13.6; 11.5; 6.85; 4.74. FAB-MS: 363 ([*M* + H]$^+$), 239, 209, 137, 109, 87. HR-FAB-MS: 363.2698 ([*M* + Na]$^+$, $C_{20}H_{40}NaO_2Si^+$; calc. 363.2695).

*(4*R*S,5*S*,6*R*,7*E*,9*E*)-Isomer* (*ent-anti-***13**). In the same manner as described for *anti-***13**, *ent-anti-***12** (618 mg, 1.73 mmol) afforded *ent-anti-***13** (246 mg, 0.71 mmol, 42% in two steps). Colorless oil. HR-FAB-MS: 363.2701 ([*M* + Na]$^+$, $C_{20}H_{40}NaO_2Si^+$; calc. 363.2695).

Compound anti-**9** *from* anti-**13**. To a soln. of *anti-***13** (21 mg, 0.062 mmol) in DMSO (1 ml) at r.t. were added IBX (69 mg, 0.2467 mmol) and mol. sieves (4 Å; 130 mg). After stirring for 5 h, the reaction was quenched with ice-cold H_2O, and the mixture was stirred for 10 min. It was filtered out *Celite* pad and extracted with AcOEt. The org. layer were washed with brine, dried ($MgSO_4$), filtered, and concentrated. Purification of crude product by CC (SiO_2; hexane/AcOEt 15:1) afforded *anti-***9** (20 mg, 0.059 mmol, 96%). Colorless oil. $[\alpha]_D^{24} = +16$ (*c* = 0.40, Et_2O). R_f (hexane/AcOEt 6:1) 0.67. IR (film): 3300*s*, 2950*s*, 1650*s* (C=O), 1060*s*. ^{1}H-NMR (300 MHz): 5.79 (*s*, H–C(8)); 5.38 (*q*, *J* = 6.6, H–C(10)); 4.06 (*d*, *J* = 9.6, H–C(6)); 2.79 (*dq*, *J* = 7.2, 9.6, H–C(5)) 2.46–2.54 (*m*, CH_2(3)); 1.72 (*s*, Me–C(7)); 1.70 (*s*, Me–C(9)); 1.68 (*d*, *J* = 7.8, Me(11)); 1.58 (*m*, CH_2(2)); 1.21 (*d*, *J* = 7.2, Me(1)); 0.88 (*t*, *J* = 7.5, (*Me*CH_2)$_3$Si); 0.79 (*d*, *J* = 7.2, Me–C(5)); 0.51 (*q*, *J* = 7.5, (MeC*H*$_2$)$_3$Si). ^{13}C-NMR (150 MHz): 214.4; 133.9; 132.6; 132.3; 124.5; 82.4; 49.1; 46.7; 22.6; 16.4; 16.2; 13.6; 13.5; 13.4; 11.8; 6.60; 4.47. FAB-MS: 361 ([*M* + Na]$^+$), 309, 239, 209, 185, 115 ([Et_3Si]$^+$), 87. HR-FAB-MS: 361.2542 ([*M* + Na]$^+$, $C_{20}H_{38}NaO_2Si^+$; calc. 361.2538).

*(5*S*,6*R*,7*E*,9*E*)-Isomer* (*ent-anti-***9**). In the same manner as described for *anti-***9**, *ent-anti-***13** (124 mg, 0.363 mmol) afforded *ent-anti-***9** (123 mg, 0.363 mmol, quant.). Colorless oil. $[\alpha]_D^{24} = -13$ (*c* = 0.11, Et_2O). HR-FAB-MS: 361.2541 ([*M* + Na]$^+$, $C_{20}H_{38}NaO_2Si^+$; calc. 361.2538).

Pteroenone (= *(5*R*,6*S*,7*E*,9*E*)-6-Hydroxy-5,7,9-trimethylundeca-7,9-dien-4-one*; (+)-(5*R*,6*S*)-**1**). A soln. of *anti-***9** (13 mg, 0.0384 mmol) in THF (0.5 ml) was added dropwise to a soln. TBAF/HF (pH 7; prepared by mixing 1M TBAF in THF and 47% aq. HF) at 0°. After stirring for 2 h at r.t., the mixture was poured into brine and extracted with AcOEt. The extract was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed (SiO_2; hexane/AcOEt 15:1) to give (+)-(5*R*,6*S*)-**1** (8 mg, 0.0357 mmol, 93%). Colorless oil. $[\alpha]_D^{24} = +47$ (*c* = 0.30, hexane; [2]: $[\alpha]_D = +48$ (*c* = 0.6, hexane)). R_f (hexane/AcOEt 4:1) 0.41. HPLC (column, *Daicel Chiralcel® OJ*, 4.6 × 250 mm; temp., 25°; eluent, hexane/i-PrOH 100:1 at 0.5 ml/min; detection at 234 nm): t_R 24.7 (98% ee, 96% de). ^{1}H-NMR (500 MHz, C_6D_6): 5.78 (*s*, H–C(8)); 5.40 (*q*, *J* = 6.7, H–C(10)); 4.07 (*dd*, *J* = 2.5, 9.0, H–C(6)); 2.60 (*qd*, *J* = 7.0, 9.5, H–C(5)); 2.31 (*td*, *J* = 7.3, 17.5, 1 H, CH_2(3)); 2.19 (*td*, *J* = 7.3, 17.5, 1 H, CH_2(3)); 1.71 (*s*, Me–C(7)); 1.67 (*d*, *J* = 3.5, OH); 1.65 (*s*, Me–C(9)); 1.62 (*sext.*, *J* = 7.5, CH_2(9)); 1.58 (*d*, *J* = 7.0, Me(11)); 0.84 (*t*, *J* = 7.5, Me(1)); 0.82 (3 H, *d*, *J* = 7.5, Me–C(5)). ^{1}H-NMR (500 MHz, $CDCl_3$): 5.87 (*s*, H–C(8)); 5.42 (*q*, *J* = 6.6, H–C(10)); 4.13 (*dd*, *J* = 3.3, 8.7, H–C(6)); 2.80 (*dq*, *J* = 7.2, 8.8, H–C(5)) 2.51 (*t*, *J* = 7.2, CH_2(3)); 1.76 (*s*, Me–C(7)); 1.74 (*s*, Me–C(9)); 1.68 (*d*, *J* = 6.6, Me(11)); 1.62 (*sext.*, *J* = 7.3, CH_2(2)); 0.95 (*d*, *J* = 8.8, Me–C(5)); 0.92 (*d*, *J* = 7.2, H–C(1)). ^{13}C-NMR (150 MHz, C_6D_6): 12.5 (*Me*–C(7)); 13.7 (C(1)); 13.9 (C(11)); 14.1 (*Me*–C(5)); 16.5 (*Me*–C(9)); 17.0 (C(2)); 45.6 (C(3)); 48.8 (C(5)); 81.3 (C(6)); 124.9 (C(10)); 132.4 (C(8)); 133.2 (C(9)); 134.5 (C(7)); 213.2 (C(4)). FAB-MS: 247 ([*M* + Na]$^+$), 207 ([*M* + H – H_2O]$^+$), 195, 173, 115, 93, 81. HR-EI-MS: 224.1777 ($M^{+\cdot}$, $C_{14}H_{24}O_2^+$; calc. 224.1776).

*(5*S*,6*R*,7*E*,9*E*)-6-Hydroxy-5,7,9-trimethylundeca-7,9-dien-4-one* ((–)-(5*S*,6*R*)-**1**). In the same manner as described for (5*R*,6*S*)-**1**, *ent-anti-***9** (18.6 mg, 0.0549 mmol) afforded (5*S*,6*R*)-**1** (12.3 mg, 0.0549 mmol, quant.). Colorless oil. $[\alpha]_D^{24} = -46$ (*c* = 0.13, hexane). HPLC (column, *Daicel Chiralcel® OJ*, 4.6 × 250 mm; temp., 25°; eluent, hexane/i-PrOH 100:1 at 0.5 ml/min; detection at 234 nm): t_R 22.6 (99% ee, 96% de). HR-EI-MS: 224.1674 ($M^{+\cdot}$, $C_{14}H_{24}O_2^+$; calc. 224.1776).

*(4*S*)-4-Benzyl-3-[(2*S*,3*S*,4*E*,6*E*)-3-hydroxy-2,4,6-trimethylocta-4,6-dienoyl]-1,3-oxazolidin-2-one* (*syn-***5**). To a soln. of (*S*)-**2** (789 mg, 3.38 mmol) in 10 ml of CH_2Cl_2 at 0° under N_2 was added Bu_2BOTf (3.7 ml, 3.7 mmol), followed by Et_3N (0.54 ml, 3.86 mmol). The mixture was cooled to –78° and **3** (400 mg, 3.22 mmol) was added. The mixture was stirred for 30 min at this temp. and gradually warmed to

0°. After 6 h, the reaction was quenched by the addition of 20 ml of phosphate buffer (pH 7)/MeOH 1:1, followed by addition of 20 ml of 30% aq. H_2O_2/MeOH 1:1, and the mixture was stirred vigorously for 1 h. The mixture was evaporated to remove MeOH and extracted twice with CH_2Cl_2, and the combined org. layers were washed with brine, and dried ($MgSO_4$). It was filtered and concentrated under reduced pressure. Purification of crude product by CC (SiO_2; hexane/AcOEt 6:1 to 3:1) afforded *syn*-**5** (862 mg, 2.41 mmol, 75%). Colorless oil. $[\alpha]_D^{24} = +73$ ($c = 0.50$, Et_2O). R_f (hexane/AcOEt 3:1) 0.33. HPLC (column, *Daicel Chiralcel ®OD*, 4.6 × 250 mm; temp., 25°; eluent, hexane/i-PrOH 4:1 at 0.5 ml/min; detection at 254 nm): t_R 17.7 (> 99% dr). IR (KBr): 3500*s* (OH), 2900*m*, 1780*s* (C=O), 1700*s* (C=O), 1390*s*, 1210*s*. ^{1}H-NMR (300 MHz): 7.20–7.37 (*m*, 5 arom. H); 6.02 (*s*, H–C(5′)); 5.40 (*q*, $J = 6.9$, H–C(7′)); 4.65–4.74 (*m*, H–C(4)); 4.36–4.40 (*m*, H–C(3′)); 4.16–4.22 (*m*, CH_2(5)); 4.02 (*dq*, $J = 7.2$, 3.9, H–C(2′)); 3.28 (*dd*, $J = 13.5$, 3.3, 1 H, PhCH_2); 2.80 (*dd*, $J = 13.5$, 9.6, 1 H, PhCH_2); 2.78 (*d*, $J = 3.0$, OH); 1.75 (*s*, Me–C(4′)); 1.74 (*s*, Me–C(6′)); 1.68 (*d*, $J = 6.6$, Me(8′)); 1.21 (*d*, $J = 7.2$, Me–C(2′)). EI-MS: 357 ($M^{+\bullet}$), 339 ([$M - H_2O$]$^+$), 233, 177, 91. HR-EI-MS: 357.1938 ($M^{+\bullet}$, $C_{21}H_{27}NO_4^+$; calc. 357.1940).

*(4*R*,2′*R*,3′*R*,4′*E*,6′*E*)*-**5** (*ent-syn*-**5**). In the same manner as described for *syn*-**5**, **3** (463 mg, 3.73 mmol) afforded *ent-syn*-**5** (1.08 g, 3.02 mmol, 85%). Colorless oil. $[\alpha]_D^{24} = -74$ ($c = 0.24$, Et_2O). HPLC: t_R 16.5 (> 99% dr). HR-FAB-MS: 380.1838 ([$M + Na$]$^+$, $C_{21}H_{27}NNaO_4^+$; calc. 380.1838). Anal. calc. for $C_{21}H_{27}NO_4$: C 70.57, H 7.88, N 3.84; found: C 70.57, H 7.81, N 3.99.

*(2*S*,3*S*,4*E*,6*E*)-3-Hydroxy*-N-*methoxy*-N*,2,4,6-tetramethylocta-4,6-dienamide* (*syn*-**6**). To a suspension of MeONHMe · HCl (205 mg, 2.10 mmol) in dry THF (1.6 ml) was added a soln. of Me_3Al in hexane (1.0M, 2.1 ml, 2.1 mmol) at 0°, and the mixture was stirred at 20° for 15 min under N_2. The soln. was cooled to −20° before the addition of **5** (250 mg, 0.699 mmol) in dry THF (1.7 ml), and the mixture was stirred at 20° for 9 h. The reaction was quenched with 0.5M aq. HCl, and the mixture was extracted with CH_2Cl_2. The extract was washed with sat. aq. $NaHCO_3$ soln. and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified with prep. TLC (SiO_2; hexane/AcOEt 4:1) to give *syn*-**6** (138 mg, 0.572 mmol, 82%). Colorless oil. $[\alpha]_D^{26} = -19$ ($c = 0.29$, $CHCl_3$). R_f (toluene/AcOEt 3:1) 0.40. FT-IR: 3400*s* (br., OH), 1738*s* (C=O), 1641*s*, 1071*m*, 1003*s*, 741*s*. ^{1}H-NMR (600 MHz): 6.06 (*s*, 0.8 H of H–C(5)); 6.04 (*s*, 0.2 H of H–C(5)); 5.39 (*q*, $J = 6.7$, 0.8 H of H–C(7)); 5.33 (*q*, $J = 6.5$, 0.2 H of H–C(7)); 4.35 (*s*, 0.2 H); 4.29 (*s*, 0.8 H); 4.00 (*s*, 0.2 H); 3.93 (*s*, 0.8 H); 3.73 (*s*, 0.6 H of MeO); 3.72 (*s*, 2.4 H of MeO); 3.21 (*s*, 2.4 H of MeN); 3.11 (*s*, 0.6 H of MeN); 1.74 (*s*, Me); 1.73 (*s*, 2.4 H of Me); 1.68 (*d*, $J = 6.6$, 2.4 H of Me(8)); 1.55 (*s*, 0.6 H of Me); 1.51 (*d*, $J = 6.6$, 0.6 H of Me(8)); 1.15 (*d*, $J = 7.1$, 0.6 H of Me–C(2)); 1.11 (*d*, $J = 7.0$, 2.4 H of Me–C(2)). EI-MS: 241 ($M^{+\bullet}$), 224, 135, 117. HR-EI-MS: 241.1679 ($M^{+\bullet}$, $C_{13}H_{23}NO_3^+$; calc. 241.1678).

*(2*S*,3*S*,4*E*,6*E*)*-N-*Methoxy*-N*,2,4,6-tetramethyl-3-[(triethylsilyl)oxy]octa-4,6-dienamide* (*syn*-**8**). To a soln. of *syn*-**6** (34 mg, 0.14 mmol) in CH_2Cl_2 (0.5 ml) was successively added 2,6-lutidine (0.020 ml, 18 mg, 0.17 mmol) and TESOTf (0.035 ml, 40 mg, 0.16 mmol) at −30°, and the mixture was stirred for 12 h. The reaction was quenched with H_2O. The aq. layer was extracted with Et_2O, and the combined org. layers were washed with brine, dried ($MgSO_4$), filtered, and concentrated. Purification of the crude product by CC (SiO_2; hexane/AcOEt 10:1) afforded *syn*-**8** (39 mg, 0.11 mmol, 79%). Colorless oil. $[\alpha]_D^{26} = +17$ ($c = 0.71$, $CHCl_3$). R_f (hexane/AcOEt 2:1) 0.56. FT-IR: 1664*s* (C=O), 1411*m*, 1063*s*, 996*s*, 726*s*. ^{1}H-NMR (500 MHz): 5.75 (*s*, H–C(5)); 5.30 (*q*, $J = 6.6$, H–C(7)); 4.25 (*d*, $J = 9.1$, 0.2 H of H–C(3)); 4.13 (*d*, $J = 9.1$, 0.8 H of H–C(3)); 3.65 (*s*, 0.6 H of MeO); 3.64 (*s*, 2.4 H of MeO); 3.19 (br. *s*, H–C(2)); 3.10 (*s*, MeN); 1.73 (*s*, 2.4 H of Me); 1.68 (*s*, 0.6 H of Me); 1.66 (*s*, Me); 1.65 (*d*, $J = 6.6$, Me(8)); 1.22 (*d*, $J = 6.8$, 0.6 H of Me–C(2)); 1.21 (*d*, $J = 6.8$, 2.4 H of Me–C(2)); 0.96 (*t*, $J = 8.1$, 1.8 H of ($MeCH_2$)$_3$Si); 0.95 (*t*, $J = 8.1$, 7.2 H of ($MeCH_2$)$_3$Si); 0.62 (*q*, $J = 8.1$, 1.2 H of (MeCH_2)$_3$Si); 0.60 (*q*, $J = 8.1$, 4.8 H of (MeCH_2)$_3$Si). EI-MS: 355 ($M^{+\bullet}$), 326 ([M − Et]$^+$), 295 ([M − NMeOMe]$^+$), 239 ([M − MeCHC(=O)NMeOMe]$^+$), 115, 87. HR-EI-MS: 355.2543 ($M^{+\bullet}$, $C_{19}H_{37}NO_3Si^+$; calc. 355.2543).

*(4*S*)-4-Benzyl-3-{(2*S*,3*S*,4*E*,6*E*)-2,4,6-trimethyl-3-[(triethylsilyl)oxy]octa-4,6-dienoyl}-1,3-oxazolidin-2-one* (*syn*-**10**). A soln. of *syn*-**5** (400 mg, 1.12 mmol) at −55° in CH_2Cl_2 (7 ml) was treated with 2,6-lutidine (156 µl), followed by TESOTf (303 µl, 1.34 mmol). After 75 min, the reaction was quenched by H_2O. The aq. layer was extracted with Et_2O, and the combined org. layers were washed with brine, dried ($MgSO_4$), filtered, and concentrated. Purification of the crude product by CC (SiO_2; hexane/AcOEt 6:1) afforded *syn*-**10** (418 mg, 0.886 mmol, 79%). Colorless oil. $[\alpha]_D^{24} = +64$ ($c = 2.0$, Et_2O). R_f (hexane/AcOEt 3:1) 0.62. IR (film): 2950*m*, 1780*s* (C=O), 1700*s* (C=O), 1380*s*, 1210*s*, 1080*s*, 740*s*. ^{1}H-NMR

(300 MHz): 7.20–7.37 (*m*, 5 arom. H); 5.79 (*s*, H–C(5′)); 5.32 (*q*, *J* = 6.6, H–C(7′)); 4.51 (*dddd*, *J* = 9.6, 7.5, 3.3, 2.4, H–C(4)); 4.24 (*d*, *J* = 7.8, H–C(3′)); 4.03–4.15 (*m*, CH_2(5), H–C(2′)); 3.27 (*dd*, *J* = 13.2, 3.3, 1 H, PhCH_2); 2.75 (*dd*, *J* = 13.2, 9.9, 1 H, PhCH_2); 1.73 (*d*, *J* = 1.2, Me–C(4′)); 1.69 (*s*, Me–C(6′)); 1.65 (*d*, *J* = 6.9, Me(8′)); 1.24 (*d*, *J* = 6.9, Me–C(2′)); 0.94 (*t*, *J* = 8.1, (*Me*CH_2)$_3$Si); 0.58 (*q*, *J* = 8.1, (MeCH_2)$_3$Si). EI-MS: 471 ($M^{+\bullet}$), 442 ([*M* – Et]$^+$), 339 ([*M* – TESOH]$^+$), 318, 294, 262 239, 200, 115, 91. HR-EI-MS: 471.2805 ($M^{+\bullet}$, $C_{27}H_{41}NO_4Si^+$; calc. 471.2804).

*(4*R*,2′*R*,3′*R*,4′*E*,6′*E*)-Isomer* (*ent-syn-***10**). In the same manner as described for *syn-***10**, *ent-syn-***5** (730 mg, 2.04 mmol) afforded *ent-syn-***10** (962 mg, 2.04 mmol, quant.). Colorless oil. $[\alpha]_D^{24} = -59$ (*c* = 0.55, Et_2O). HR-FAB-MS: 494.2709 ([*M* + Na]$^+$, $C_{27}H_{41}NNaO_4Si^+$; calc. 494.2702).

S-*Ethyl (2*S*,3*S*,4*E*,6*E*)-2,4,6-Trimethyl-3-[(triethylsilyl)oxy]octa-4,6-dienethioate* (*syn-***11**). To a soln. of EtSH (179 µl, 2.42 mmol) in THF (9 ml) was added dropwise BuLi in hexane (1.6M, 1.0 ml, 1.615 mmol) at –78° under Ar, and the mixture was stirred for 15 min. Then, to the mixture was added a soln. of *syn-***10** (164 mg, 0.35 mmol) in THF (2 ml). The mixture was gradually warmed to 0° and stirred with sat. aq. $NaHCO_3$ soln., and the resulting mixture was extracted with Et_2O. The combined extract was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo*. CC (SiO_2; hexane/AcOEt 10:1) gave *syn-***11** (288 mg, 0.808 mmol, quant.). Colorless oil. $[\alpha]_D^{24} = +47$ (*c* = 0.43, Et_2O). R_f (hexane/AcOEt 6:1) 0.61. IR (film): 2950*m*, 2875*s*, 1680*s* (C=O), 1460*s* (C=O), 1240*s*, 1080*s*, 1000*s*, 960*s*, 740*s*. ^{1}H-NMR (300 MHz): 5.74 (*s*, H–C(5)); 5.33 (*q*, *J* = 6.6, H–C(7)); 4.15 (*d*, *J* = 7.2, H–C(3)); 2.77–2.88 (*m*, MeCH_2S); 2.72 (*dq*, *J* = 9.0, 7.5, H–C(2)); 1.74 (*s*, Me–C(4)); 1.67 (*s*, Me–C(6)); 1.66 (*d*, *J* = 9.9, Me(8)); 1.20 (*d*, *J* = 7.2, Me–C(2)); 1.19 (*t*, *J* = 7.2, *Me*CH_2S); 0.93 (*t*, *J* = 7.8, (*Me*CH_2)$_3$Si); 0.57 (*q*, *J* = 7.8, (MeCH_2)$_3$Si). ^{13}C-NMR (150 MHz): 201.8; 134.3; 132.8; 131.4; 124.2; 80.4; 53.5; 23.0; 16.4; 14.6; 13.7; 13.6; 13.0; 6.83; 6.79; 6.38; 4.77. EI-MS: 356 ($M^{+\bullet}$), 327 ([*M* – Et]$^+$), 291, 239, 217, 189, 161, 133, 115 ([Et_3Si]$^+$), 87. HR-EI-MS: 356.2207 ($M^{+\bullet}$, $C_{19}H_{36}O_2SSi^+$; calc. 356.2205).

*(2*R*,3*R*,4*E*,6*E*)-Isomer* (*ent-syn-***11**). In the same manner as described for *syn-***11**, *ent-syn-***10** (681 mg, 1.44 mmol) afforded *ent-syn-***11** (514 mg, 1.44 mmol, quant.). Colorless oil. $[\alpha]_D^{24} = -44$ (*c* = 0.25, Et_2O). HR-FAB-MS: 357.2288 ([*M* + H]$^+$, $C_{19}H_{37}O_2SSi^+$; calc. 357.2284).

*(2*S*,3*S*,4*E*,6*E*)-2,4,6-Trimethyl-3-[(triethylsilyl)oxy]octa-4,6-dienal* (*syn-***12**). A flask was charged with *syn-***11** (90 mg, 0.252 mmol) in dry CH_2Cl_2 (1.5 ml) at –80°. To the soln. was added DIBAL in hexane (0.94M, 0.28 ml, 0.265 mmol). After 20 min, the mixture was stirred with aq. *Rochelle* salt soln., then extracted with Et_2O. The combined extract was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo* to give *syn-***12** (74 mg, 0.250 mmol, 99%). Colorless oil. $[\alpha]_D^{24} = -8.0$ (*c* = 1.0, Et_2O). R_f (hexane/AcOEt 6:1) 0.52. IR (film): 2950*m*, 2855*s*, 1725*s* (C=O), 1060*s*. ^{1}H-NMR (300 MHz): 9.69 (*d*, *J* = 2.1, H–C(1)); 5.87 (*s*, H–C(5)); 5.36 (*q*, *J* = 6.9, H–C(7)); 4.31 (*d*, *J* = 6.6, H–C(3)); 2.54 (*quint.*, *J* = 6.9, H–C(2)); 1.72 (*s*, Me–C(4)); 1.72 (*s*, Me–C(6)); 1.68 (*d*, *J* = 6.9, Me(8)); 1.05 (*d*, *J* = 6.9, Me–(2)); 0.94 (*t*, *J* = 8.4, (*Me*CH_2)$_3$Si); 0.58 (*q*, *J* = 7.5, (MeCH_2)$_3$Si). ^{13}C-NMR (150 MHz): 204.7; 133.9; 132.7; 130.9; 124.6; 78.1; 51.0; 23.0; 16.5; 14.1; 13.6; 8.96; 6.80; 4.77. EI-MS: 296 ($M^{+\bullet}$), 267 ([*M* – Et]$^+$), 239, 217, 115 ([Et_3Si]$^+$), 87. HR-EI-MS: 296.2178 ($M^{+\bullet}$, $C_{17}H_{32}O_2Si^+$; calc. 296.2172).

*(4*RS*,5*R*,6*S*,7*E*,9*E*)-5,7,9-Trimethyl-6-[(triethylsilyl)oxy]undeca-7,9-dien-4-ol* (*syn-***13**). To a soln. of *syn-***12** (31 mg, 0.10 mmol) in Et_2O (1.0 ml) was added PrLi in Et_2O (1.3M, 160 µl, 0.273 mmol) at –80° under Ar, and the mixture was stirred for 30 min. The reaction was quenched with sat. aq. NH_4Cl soln., and the resulting mixture was extracted with Et_2O. The combined extract was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo*. Purification of the crude product by TLC (hexane/AcOEt 50:1) afforded *syn-***13** (22 mg, 0.065 mmol, 65%). Colorless oil. R_f (hexane/AcOEt 6:1) 0.54. IR (film): 3450*s* (br., OH), 2880*s*, 1460*s*, 1000*s*. ^{1}H-NMR (300 MHz): 5.85 (*s*, H–C(8)); 5.36 (*q*, *J* = 6.9, H–C(10)); 4.05 (*d*, *J* = 6.3, H–C(6)); 3.50–3.60 (*m*, H–C(4)) 2.13 (*d*, *J* = 3.3, OH); 1.73 (*s*, Me–C(7)); 1.69 (*d*, *J* = 6.9, Me(11)); 1.69 (*s*, Me–C(9)); 1.26–1.54 (*m*, CH_2(3), CH_2(2), H–C(5)); 0.95 (*t*, *J* = 7.8, (*Me*CH_2)$_3$Si); 0.95 (*t*, *J* = 7.8, Me(1)); 0.88 (*d*, *J* = 6.9, Me–C(5)); 0.62 (*q*, *J* = 7.8, (MeCH_2)$_3$Si). ^{13}C-NMR (150 MHz): 135.2; 133.0; 130.2; 124.1; 82.4; 73.2; 65.8; 40.7; 37.4; 19.3; 16.6; 15.3; 14.2; 14.1; 13.6; 7.01; 6.87; 4.85. FAB-MS: 339 ([*M* – H]$^-$), 306, 199, 153, 131. HR-FAB-MS: 339.2719 ([*M* – H]$^-$, $C_{20}H_{39}O_2Si^-$; calc. 339.2719).

*(4*RS*,5*R*,6*S*,7*E*,9*E*)-Isomer* (*ent-syn-***13**). In the same manner as described for *syn-***12** and *syn-***13**, *ent-syn-***11** (489 mg, 1.37 mmol) afforded *ent-syn-***13** (233 mg, 0.685 mmol, 50% in two steps). Colorless oil. HR-FAB-MS: 363.2697 ([*M* + Na]$^+$, $C_{20}H_{40}NaO_2Si^+$; calc. 363.2695).

(5S,6S,7E,9E)-5,7,9-Trimethyl-6-[(triethylsilyl)oxy]undeca-7,9-dien-4-one (*syn*-**9**). To a soln. of *syn*-**13** (18 mg, 0.0528 mmol) in DMSO (1 ml) at r.t. were added IBX (59 mg, 0.21 mmol) and mol. sieves (4 Å; 130 mg). After stirring for 7 h, the reaction was quenched by ice-cold H_2O, and the mixture stirred for 10 min. It was filtered out *Celite* pad and extracted with AcOEt. The org. layer were washed with brine, dried ($MgSO_4$), filtered, and concentrated. Purification of crude product by CC (SiO_2; hexane/AcOEt 15:1) afforded *syn*-**9** (17.5 mg, 0.0517 mmol, 98%). Colorless oil. $[\alpha]_D = +13.2$ ($c = 1.25$, Et_2O). R_f (hexane/AcOEt 6:1) 0.63. IR (film): 3400*s* (br.), 2950*s*, 1700*s* (C=O), 1080*s*, 1000*s*. ^{1}H-NMR (300 MHz): 5.72 (*s*, H−C(8)); 5.31 (*q*, $J = 6.3$, H−C(10)); 4.09 (*d*, $J = 8.1$, H−C(6)); 2.78 (*dq*, $J = 6.9$, 8.4, H−C(5)) 2.35 (*t*, $J = 6.9$, CH_2(3)); 1.72 (*s*, Me−C(7)); 1.67 (*s*, Me−C(9)); 1.66 (*d*, $J = 6.9$, Me(11)); 1.52 (*sext.*, $J = 6.9$, CH_2(2)); 1.10 (*d*, $J = 6.6$, Me−C(5)); 0.93 (*t*, $J = 8.1$, (*Me*CH_2)$_3$Si); 0.87 (*t*, $J = 7.5$, Me(1)); 0.58 (*q*, $J = 7.8$, (MeC*H*$_2$)$_3$Si). ^{13}C-NMR (150 MHz): 213.4; 134.6; 132.7; 131.2; 124.3; 80.3; 51.2; 44.9; 22.6; 16.7; 13.7; 13.6; 13.4; 13.1; 6.84; 4.78. FAB-MS: 339 ($[M+H]^+$), 239, 227, 209, 137, 115 ($[Et_3Si]^+$), 87. HR-FAB-MS: 339.2716 ($[M+H]^+$, $C_{20}H_{39}O_2Si^+$; calc. 339.2719).

(5R,6R,7E,9E)-Isomer (*ent-syn*-**9**). In the same manner as described for *syn*-**13**, *ent-syn*-**13** (60.8 mg, 0.178 mmol) afforded *ent-syn*-**9** (52.8 mg, 0.156 mmol, 88%). Colorless oil. $[\alpha]_D^{24} = -12$ ($c = 0.15$, Et_2O). HR-FAB-MS: 361.2543 ($[M+Na]^+$, $C_{20}H_{38}NaO_2Si^+$; calc. 361.2538).

(5S,6S,7E,9E)-6-Hydroxy-5,7,9-trimethylundeca-7,9-dien-4-one ((−)-(5*S*,6*S*)-**1**). A soln. of *syn*-**9** (15 mg, 0.0443 mmol) in THF (0.5 ml) was added dropwise to a soln. TBAF/HF (pH 7; prepared by mixing 1M TBAF in THF and 47% aq. HF) at 0°. After stirring for 30 min at 0°, the mixture was poured into brine and extracted with AcOEt. The extract was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was submitted to CC (SiO_2; hexane/AcOEt 15:1) to give (5*S*,6*S*)-**1** (7 mg, 0.0312 mmol, 70%). Colorless oil. $[\alpha]_D^{24} = -66$ ($c = 0.045$, hexane). R_f (hexane/AcOEt 4:1) 0.30. HPLC (column, *Daicel Chiralcel® OJ*, 4.6 × 250 mm; temp., 25°; eluent, hexane/i-PrOH 100:1 at 0.5 ml/min; detection at 234 nm): t_R 19.6 (96% ee, 91% de). IR (film): 3420*s* (OH), 2950*s*, 1700*s* (C=O), 1450*m*, 1020*m*. ^{1}H-NMR (300 MHz, C_6D_6): 6.14 (*s*, H−C(8)); 5.42 (*qt*, $J = 6.9$, 1.3, H−C(10)); 4.22 (*pseudo-d*, $J = 4.0$, H−C(6)); 2.48 (*qd*, $J = 7.1$, 4.9, H−C(5)); 2.27 (*d*, $J = 2.7$, OH); 2.04 (*td*, $J = 6.8$, 1.6, CH_2(3)); 1.68 (*pseudo-s*, Me); 1.65 (*d*, $J = 1.3$, Me); 1.59 (*d*, $J = 6.9$, Me(11)); 1.51 (*sext.*, $J = 7.4$, CH_2(2)); 1.04 (*d*, $J = 7.1$, Me−C(5)); 0.78 (*t*, $J = 7.5$, Me(1)). ^{1}H-NMR (300 MHz, $CDCl_3$): 5.95 (*s*, H−C(8)); 5.37 (*q*, $J = 6.6$, H−C(10)); 4.32 (br. *s*, H−C(6)); 2.76 (*dq*, $J = 7.2$, 4.5, H−C(5)); 2.48 (*t*, $J = 7.2$, CH_2(3)); 1.72 (*s*, Me−C(7), Me−C(9)); 1.68 (*d*, $J = 6.9$, Me(11)); 1.60 (*sext.*, $J = 7.2$, CH_2(2)); 1.08 (*d*, $J = 7.2$, Me−C(5)); 0.92 (*d*, $J = 7.2$, Me(1)). ^{13}C-NMR (75 MHz, C_6D_6): 213.8; 134.1; 133.7; 130.6; 124.4; 76.6; 49.1; 43.8; 17.1; 16.9; 14.8; 13.9; 13.7; 10.8. ^{13}C-NMR (125 MHz): 215.4; 132.9; 132.8; 130.1; 124.4; 75.9; 48.5; 43.8; 16.9; 16.7; 15.0; 13.72; 13.66; 10.3. FAB-MS: 247 ($[M+Na]^+$), 207, 125, 124, 71. HR-EI-MS: 224.1776 ($M^{+\bullet}$, $C_{14}H_{24}O_2^+$; calc. 224.1776).

(5R,6R,7E,9E)-6-Hydroxy-5,7,9-trimethylundeca-7,9-dien-4-one ((+)-(5*R*,6*R*)-**1**). In the same manner as described for (5*S*,6*S*)-**1**, *ent-syn*-**9** (3.2 mg, 0.0082 mmol) afforded (5*R*,6*R*)-**1** (1.6 mg, 0.0071 mmol, 87%). Colorless oil. $[\alpha]_D^{24} = +66$ ($c = 0.125$, hexane). HPLC: t_R 18.9 (98% ee, 90% de). HR-FAB-MS: 247.1677 ($[M+Na]^+$, $C_{14}H_{24}NaO_2^+$; calc. 247.1674).

Bioassay. Antifeedant activity of four diastereoisomers against a benthic fish (*Notothenia coriiceps*) collected near Palmer Station, Anvers Island, on the western Antarctic Peninsula, was tested according to the method described in [1b].

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