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# Alternative Synthesis of the Colorado Potato Beetle Pheromone

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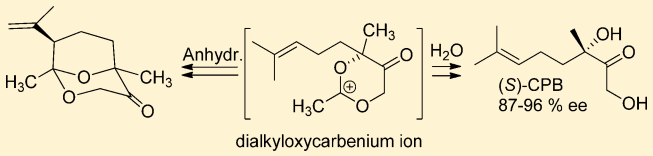
Supporting Information

**ABSTRACT:** A concise preparation of the pheromone secreted by the male Colorado potato beetle [viz. (3*S*)-1,3-dihydroxy-3,7-dimethyl-6-octen-2-one] was accomplished in four steps starting from 2-fluoronerol or 2-fluorogeraniol. The key step in the synthesis involves a 6-endo epoxide ring-opening with ester participation that simultaneously inverts the 3*R*-configuration of the (3*R*)-2,3-epoxy-2-fluoroprenyl acetate intermediate and installs the ketone functionality of the semiochemical. Extensive NMR studies validate the proposed 6-endo mechanism of the featured rearrangement, which under anhydrous conditions resulted in the formation of two bicyclic 1,3-dioxan-5-ones via an unprecedented intramolecular Prins cyclization.

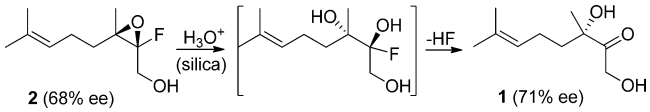



The Colorado potato beetle (CPB), *Leptinotarsa decemlineata* [Say], is a severe defoliator of potatoes and one of the most economically significant pests affecting food crops of the Solanaceae family globally.[1] Control of the CPB has relied on the heavy use of synthetic insecticides,[2] which has led to the development of insecticide-resistant populations worldwide.[3] To reduce the overall use of harmful and expensive insecticides, new pest management strategies, based on the deployment of natural host plant attractants or synthetic kairomone blends, have been explored to combat CPB infestations. The recent discovery of a male-produced aggregation pheromone of CPB,[4] identified as (3*S*)-1,3-dihydroxy-3,7-dimethyl-6-octen-2-one (**1**),[5] has made possible the formulation of a potent attractant for pest management of CPB.[6,7]

Preliminary bioassays established that while (*S*)-**1**, which is only produced by males, was able to attract both sexes of *L. decemlineata*, its enantiomer, (*R*)-**1**, not only lacked attractivity, but blocked the effects of (*S*)-**1**,[8] thereby providing an impetus for the stereoselective synthesis of the latter. In the initial report, the desired chirality was obtained in six steps from naturally occurring (*S*)-linalool.[5] Shortly thereafter, a gram-scale enantioselective synthesis was published in which the chirality at C3 was introduced by lipase-catalyzed resolution of racemic (±)-2,3-epoxynerol.[9]

The present work was sparked by the isolation of pheromone **1** as a side product (10−12%) during the silica gel purification of fluoro epoxide (2*R*,3*R*)-**2** (68% ee, Scheme 1), a synthetic intermediate required in pilot experiments to prepare[10] (*R*)-2-fluorolinalool,[11,12] and its diphosphate derivative[13] for mechanistic and structural studies with several monoterpene cyclases.[11,14] Although this decomposition could be prevented by addition of 10% triethylamine to the chromatography solvent, interestingly, chiral GC analysis[5,9] of the rearranged diol[15,16] **1** (71% ee) indicated the same 3*S*-chirality as the natural pheromone (Scheme 1), thus opening the possibility of a novel enantioselective synthesis of the CPB pheromone by asymmetric epoxidation of 2-fluoronerol or 2-fluorogeraniol.[17] Although the isolated yield of (*S*)-**1** could only be increased to a maximum of 15% upon adsorption of epoxide (2*R*, 3*R*)-**2** on silica gel (1−5 h), this one-step enantioselective synthesis of **1** from known 2-fluoronerol[11] compares favorably with those previously reported starting from geraniol/linalool (seven/six steps)[5] or nerol (six steps)[9] and hence prompted us to develop a more reliable synthesis of CPB pheromone in solution. Recently, a different synthetic approach to (*S*)-**1** has been reported starting from (*R*)-glyceraldehyde acetonide (seven steps, 47% overall yield).[18]

**Scheme 1. Stereoselective Solvolysis of Epoxide 2 on silica gel**




Previous studies with optically active 2,3-epoxygeranyl and 2,3-epoxyneryl acetates have shown that under acid-catalyzed solvolytic conditions ($HClO_4$/DMF) the epoxide ring is intermolecularly opened with net inversion of configuration at the tertiary γ-position (Scheme 2, panel A).[5,9,19] It seemed reasonable that in the absence of a nucleophilic solvent ($H_2O$ or DMF), intramolecular ring-opening with assistance of the ester group would predominate and might allow better control of the reaction. However, depending on whether the initial cyclization follows a 6-*endo* or a 5-*exo* mechanism (Scheme 2, panel B), the 3-position of **3** would undergo inversion or retention, respectively.

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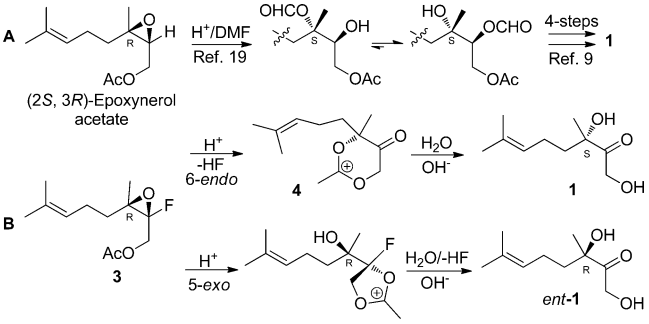
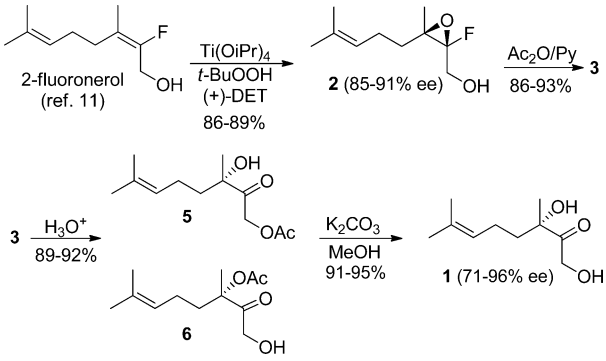
**Scheme 2. Previous Synthesis of Pheromone 1 from (2*S*,3*R*)-2,3-Epoxynerol Acetate (Panel A) and Predicted Stereochemical Course of the Fluoro Epoxy Ester Rearrangement Following 6-*Endo* or 5-*Exo* Cyclizations (Panel B)**




While acid-catalyzed epoxide-ring-opening reactions with neighboring ester participation[20] are known to occur with inversion of configuration via discrete dialkoxycarbenium ions[21] (e.g., **4**, Scheme 2) and $S_N2$-like transition states,[22] typically 5-*exo* cyclizations are preferred for $\beta$-epoxy esters,[22d] although in some instances alkyl substitution at the distal center of $\beta$- or $\gamma$-epoxy esters has been shown to promote *endo*-cyclizations.[20] However, $\alpha$-fluoro epoxides react preferentially at the non-fluorinated carbon,[16e,17] and hence the intrinsic effect of fluorine substitution might be expected to overcome the factors that would ordinarily favor 5-*exo* cyclizations (panel B, Scheme 2).

The enantioselective synthesis of the (*S*)-CPB pheromone (**1**) starting from known 2-fluoronerol is outlined in Scheme 3.

**Scheme 3. Synthesis of Pheromone 1 from 2-Fluoronerol**

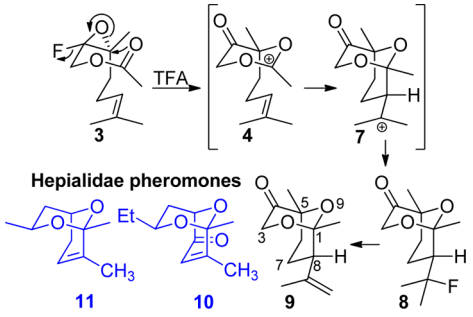



Both 2-fluoronerol and 2-fluorogeraniol are easily prepared via Horner–Emmons–Wadsworth olefination of 6-methyl-5-hepten-2-one using triethyl fluorophosphonoacetate, and subsequent $LiAlH_4$ reduction of the resulting 1:1 mixture of *cis* and *trans*-fluoro esters.[11] In the present study, epoxidation of 2-fluoronerol under standard Sharpless asymmetric (SAE) conditions [$Ti(OiPr)_4$, 1 equiv; L-(+)-diethyl tartrate, 1 equiv; *t*-BuOOH (TBHP), 2 equiv; −20 °C, overnight],[23] led to (2*R*,3*R*)-**2** in moderate yield (54%) and enantiopurity (**2**, 68% ee). The (2*R*,3*R*)-configuration of the fluorinated epoxy alcohol **2** was ascertained on the basis of the exclusive isolation of the $SiO_2$-promoted hydrolysis product diol (**1**, 71% ee) with the (3*S*)-configuration (vide supra). Hence, the enantioselection observed in the epoxidation of 2-fluoronerol with (+)-diethyl tartrate parallels that of nerol under SAE conditions. Gratifyingly, lower temperatures (−40 and −60 °C) and extended reaction times (48–72 h) led to the production of (2*R*,3*R*)-**2** in higher enantiomeric excess (85–91%) and improved, synthetically useful yields (86–89%). This temperature-dependent asymmetric induction has been previously observed with similar fluorinated allylic alcohols.[17b]

After acetylation ($Ac_2O$/Py, 86–93%), exposure of the resulting epoxy acetate **3** to catalytic amounts of trifluoroacetic acid (TFA) in benzene (0.1–0.3% $H_2O$) gave a ca. 3:2 mixture of acetates **5** and **6** ($t_{1/2}$ = 300 min), which upon deacetylation ($K_2CO_3$/MeOH, 91–95%) led to the CPB pheromone **1** in good overall yield (66%) and high ee (96% ee). The optical rotation measured for **1** [$[\alpha]^{25}_D$ = +3.2 (*c* 0.4, $CHCl_3$)] was consistent with the literature value [$[\alpha]^{25}_D$ = +3.8 (*c* 0.9, $CHCl_3$)],[9] thereby providing further confirmation of its absolute (3S)-configuration. Interestingly, a much faster fluoro epoxy rearrangement (**3** → **5** + **6**) was observed on silica gel, and after a loading time of only 30 min, acetate **3** (85% ee) was converted to a 1:2 mixture of esters **5** and **6** in 84% yield. Deacetylation ($K_2CO_3$/MeOH, 87%) of this mixture provided diol (*S*)-**1** in 87% ee and 60% overall yield. An identical enantioselective synthesis of **1** (70% ee, 68% overall yield) was accomplished from the isomeric 2-fluorogeraniol by standard (−20 °C, 16 h) Sharpless asymmetric epoxidation using D-(−)-diethyl tartrate.

The isolation of the rearranged product as a mixture of primary and tertiary acetates (**5** + **6**), combined with the substantial solvolytic acceleration observed with epoxy acetate **3** (vs epoxy alcohol **2**) on silica gel supports the anchimeric assistance of the acetate group of **3** during the solvolytic reaction. Moreover, the lack of ee erosion observed upon inversion of the (3*R*)-configuration in **3** is consistent with the intermediacy of dialkoxycarbenium ion **4** (Scheme 2) in what appears to be an exclusive 6-*endo* acid-catalyzed process. To gain further evidence in support of this mechanism, we carried out additional experiments monitored by NMR spectroscopy in the absence of moisture using (3*R*)-**3** and (±)-**3**, the latter prepared from $^{18}O$-labeled 1-$^{13}C$ acetic acid bearing both isotopes in the ester carbonyl group.

**Scheme 4. Prins Cyclization of 4 Leading to 8 and 9 and Structures of the Natural Pheromones 10 and 11**




When monitored by NMR, exposure of acetate **3** [$\delta_F$ −141.64 (t, *J* = 16.5 Hz)] to 8.5 mM TFA/$C_6D_6$ under anhydrous conditions led to a reaction ($t_{1/2}$ = 6 h) that gave a single bicyclic fluorinated product (**8**) [$\delta_F$ −127.44 ppm (br s)] that slowly decomposed to bicyclic olefin **9** via acid-catalyzed $\beta$-elimination of HF (Scheme 4).[24] Indeed, an isolated sample of **8** was shown to undergo conversion to the bicyclic ketal **9** with $t_{1/2}$ ca. 20 h at 100 mM TFA/$C_6D_6$. The structural assignments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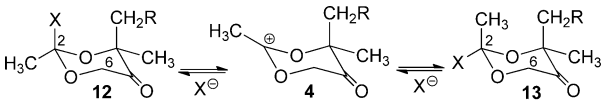
of **8** and **9** were rigorously determined by extensive 1D and 2D NMR analysis including COSY, DEPT, HSQC, HMBC, and NOESY experiments. The configuration of the isopropenyl group of **9** was determined from the *J* values (12.7 and 3.7 Hz) of the well-resolved $^{1}$H NMR signal corresponding to the C8 allylic methine hydrogen (Scheme 4). These experimental values were in good agreement with the coupling constants predicted by the Karplus equation[25] (12.1 and 3.9 Hz) using the dihedral angles (170.4 and 53.3°) to the neighboring C7 hydrogens calculated by MM2 for the exo-isomer (**9**). Similar coupling constants and calculated dihedral angles were also found for **8**. Hence, the orientation of the isopropenyl group in **9** (and the fluoropropyl group in **8**) is a consequence of the exo-orientation of the remaining double bond in **4** during the unprecedented Prins cyclization depicted in Scheme 4.

When this reaction was carried out using a sample of (±)-**3** prepared from $^{18}$O-labeled 1-$^{13}$C acetic acid and bearing both isotopes in the ester carbonyl group, unambiguous evidence for anchimeric assistance by the acetate group was obtained. Thus, the $^{18}$O-label was shown to be located in O-9 of **9** (Scheme 4) by the observation of upfield shifts in the $^{13}$C NMR signals of C-1 and C-5 ($\Delta\delta$ = 24 and 27 ppb, respectively). The isolation of **5** resulting from traces of moisture in the reaction showed that the $^{18}$O-label was located exclusively at the tertiary hydroxyl C3 position ($\Delta\delta$ = 26 ppb), thereby providing further evidence for the *6-endo* cyclization.

NMR monitoring also allowed the observation of reaction intermediates. The disappearance of the starting material (**3**) ($t_{1/2}$ = 50 min) was much faster than the formation of **8** ($t_{1/2}$ = 6 h) and yielded, upon exposure to acid, a rapid equilibrating mixture of two transient species (tentatively **12** and **13**, Scheme 5) simultaneously detected by $^{19}$F and $^{1}$H NMR during the

**Scheme 5. Equilibrating Mixture of 1,3-Dioxan-5-ones 12 and 13 via Dialkoxycarbenium Ion 4**




early stages of the rearrangement. In particular, the observed chemical shifts and coupling constants of the clear signals at $\delta_H$ 4.20 (d, *J* = 18.0 Hz), 4.19 (d, *J* = 16.8 Hz), 3.80 (d, *J* = 18.0 Hz), and 3.77 (d, *J* = 16.8 Hz) were consistent with the values reported for the geminal C6 methylene hydrogens of 2,2,4,4-tetrasubstituted 1,3-dioxan-5-ones (18−17 Hz),[26] thereby providing support for the proposed structures **12** and **13**, in equilibrium via dialkoxycarbenium ion **4** (Scheme 5). During the experiments with (±)-**3** bearing the $^{13}$C-label, monitoring by $^{13}$C NMR showed two broad signals (120.5 and 118.6 ppm) that were observed concurrently in the $^{1}$H NMR spectrum as two broad peaks at 4.2 and 3.8 ppm. These signals became sharper at 10 °C and were interpreted to arise from the C-2 of the intermediate (**12** + **13**), made observable by $^{13}$C-labeling. While the chemical shifts of these $^{13}$C NMR signals agree with the very limited values found in the literature for the quaternary carbon of related orthoacyl TFA esters[27] (X = $CF_3COO$, Scheme 5), the equal intensities of the signals could also suggest a doublet (**12** + **13**) from coupling by F ($J_{CF}$ = 240 Hz). Indeed, these values are consistent with the reported $^{13}$C NMR data for 2-fluoro-1,3-dioxolane (117.2 ppm, $J_{CF}$= 249 Hz).[28] When the reaction of **3** was monitored by $^{19}$F NMR, two unequal signals were detected at −69 and −72 ppm during the initial stages of the reaction. These came near the diagnostic sharp singlet (−77 ppm) of TFA and are consistent with the interception of dialkoxycarbenium ion **4** by TFA. At this point it is unclear whether the observed intermediates are orthoacyl TFA esters or orthoacyl fluorides (X = F, Scheme 5).

In conclusion, a straightforward, four-step enantioselective synthesis of pheromone **1** was accomplished in good overall yield (66%) and high enantiomeric excess (87−96%) starting from the easily accessible 2-fluoronerol or 2-fluorogeraniol. The key fluoro epoxy ester rearrangement was shown to proceed with anchimeric participation of acetate, thus effecting with high stereoselective control the inversion of the 3R-configuration in **3**. This simple synthetic sequence has been shown to be fully reproducible in the 30−300 mg range, and hence, it seems reasonable to expect its effective scalability, at the very least, to 1 g quantities.

Extensive NMR work with unlabeled and doubly labeled **3** revealed that the reaction proceeds via a 6-endo cyclization, and the presence of transient intermediates was detected. Depending upon reaction conditions, the initial ionic cyclization product **4** is either neutralized by a molecule of $H_2O$ yielding two acetylated variants (**5** and **6**) of the CPB pheromone (S)-**1**, or intramolecularly captured by the distal $\pi$-bond (anhydrous conditions) to give, initially, a bicyclic fluoro-containing ketal **8** that slowly decomposes to **9**. Notably, the novel pseudomonoterpene bicyclic structures **8** and **9**, synthesized here via an unprecedented intramolecular Prins cyclization of dialkoxycarbenium ion **4**, possess the 2,9-dioxabicyclo [3.3.1]non-7-ene skeleton of the pheromones **10** and **11** (Scheme 4) secreted by two different male moths of the Hepialidae family.[29] They are also structurally similar to the bicyclic ketals of the beetle pheromones brevicomin and frontalin identified by Silverstein nearly 50 years ago.[30]

## EXPERIMENTAL SECTION

**General Procedures.** Flash column chromatography was performed on 230−400 mesh silica gel. Analytical thin-layer chromatography (TLC) was carried out using commercial glass plates precoated to a depth of 0.25 mm with 230−400 mesh silica gel impregnated with a fluorescent indicator (F-254). Benzene, diethyl ether, and $CH_2Cl_2$ were dried by means of a solvent filtration system.

Optical rotations were recorded in $CHCl_3$ at 25 °C on a digital polarimeter with a Na lamp (589 nm) and an estimated error of less than ±0.2°. $^{1}$H, $^{13}$C, and $^{19}$F NMR spectra were recorded on 400, 500, and 600 MHz NMR spectrometers. Chemical shifts are expressed in parts per million ($\delta$ scale) downfield from tetramethylsilane ($CHCl_3$: $\delta_H$ 7.26; $CDCl_3$ $\delta_C$ 77.0) or ($C_6D_6$: $\delta_H$ 7.16; $C_6D_6$ $\delta_C$ 128.0). The $^{19}$F NMR spectra are unreferenced. The abbreviation "app" (apparent) in NMR data means that the interpretation was based on a first-order analysis of the multiplet in question. Commercial $CDCl_3$ was purified by filtering through basic alumina and dried overnight over molecular sieves (4 Å) in the dark. $C_6D_6$ and $CD_3CN$ were used without purification. Infrared (IR) spectra were recorded using NaCl plates and the absorbances frequencies are given as wavenumbers in $cm^{-1}$ at the peak maximum. Chiral GC analyses were carried out on a $\beta$-cyclodextrin dimethyl, 0.25 $\mu$m, 30 m × 0.32 mm) capillary column. Most products were purified by preparative TLC on silica gel with glass plates of 0.25 mm thickness. Nondestructive TLC visualizations were performed by spraying with a 0.1% solution of berberine chloride in EtOH, and UV light. The purity of purified compounds was judged to be ≥95% by TLC and/or GC analyses and NMR spectra unless otherwise specified.

For chiral GC analysis, racemic samples of 2-fluoro-2,3-epoxynerol and 2-fluoro-2,3-epoxygeraniol were prepared by Sharpless's vanadium-catalyzed *tert*-butyl hydroperoxide epoxidation.[31]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**(±)-2-Fluoro-3,7-dimethylocta-1,6-dien-3-ol ((±)-2-Fluorolinalool).** The title compound was prepared following a protocol described for the preparation of (*S*)-nerolidol.[10] To a cold (−20 °C) solution of 2-fluoro-2,3-epoxynerol (25 mg, 0.134 mmol) in anhydr $CH_2Cl_2$ (0.5 mL) was added $Et_3N$ (30 μL, 0.215 mmol) followed by methanesulfonyl chloride (12 μL, 0.155 mmol). After 1 h, the reaction was quenched by slow addition of saturated aqueous $NaHCO_3$ (1 mL). The resulting mixture was extracted with $Et_2O$ (3 × 0.5 mL), and the organic extracts were dried with anhydrous $Na_2SO_4$ overnight. Ammonia (ca. 5 mL) was collected and cooled at −78 °C as the above ethereal solution (ca. 2 mL) having the crude mesylate was added followed by the addition of Na (18.5 mg, 0.80 mmol) in small portions until the blue color remained. The mixture was allowed to warm to −40 °C (1 h) and then $NH_4Cl$ (300 mg) was added. After evaporation of $NH_3$, extractive work up using $Et_2O$ and purification on silica gel using 5−10% EtOAc-hexane gave 3,7-dimethyl-6-octen-2-one (8 mg, 39%) followed by 2-fluorolinalool (6 mg, 27%). Further elution of the column with diethyl ether gave 1-hydroxy-3,7-dimethyl-6-octen-2-one (5 mg, 22%). The undesired β-elgenone (3,7-dimethyl-6-octen-2-one) and 1-hydroxy-3,7-dimethyl-6-octen-2-one likely arise from a reductive epoxy ketone rearrangement of epoxide **2** under Birch reduction conditions.

**Data for (±)-2-fluorolinalool:** colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) δ 5.13 (1H, app tt, $J_{app}$ = 7.1, 1.5 Hz), 4.66 (1H, app dd, $J_{app}$ = 4.3, 3.2 Hz), 4.58 (1H, dd, $^3J_{H-F}$ = 28.7 Hz, and $J$ = 3.2 Hz), 1.95−2.14 (m, 3H), 1.68 (3H, s), 1.61 (3H, s), 1.37 (3H, d, $J$ = 0.9 Hz). The NMR data are in excellent agreement with the values recently reported for 2F-linanlool at 400 MHz.[11]

**Data for (±)-3,7-dimethyl-6-octen-2-one:** colorless oil; $^1$H NMR (500 MHz, $CDCl_3$) δ 5.07 (1H, t, $J$ = 7.2 Hz), 2.51 (1H, tq, $J$ = 13.9, 6.8 Hz), 2.13 (3H, s), 1.96 (2H, broad dt, $J$ = 14.8, 7.8 Hz), 1.70 (1H, m), 1.68 (3H, s), 1.59 (3H, s), 1.36 (1H, m), 1.08 (3H, dd, $J$ = 6.9, 0.7 Hz). The spectrum and $^1$H NMR values are in excellent agreement with those recently published.[32]

**Data for (±)-1-hydroxy-3,7-dimethyl-6-octen-2-one:** colorless oil; $^1$H NMR (500 MHz, $CDCl_3$) δ 5.03 (1H, tt, $J$ = 7.2, 1.5 Hz), 4.27 (2H, app dq, $J_{app}$ = 19.1, 4.6 Hz), 2.55 (1H, tq, $J$ = 13.7, 6.8 Hz), 1.96 (2H, app broad d, $J_{app}$ = 7.2 Hz), 1.70 (1H, ddt, $J$ = 13.7, 6.9, 1.7 Hz), 1.68 (3H, s), 1.58 (3H, s), 1.44 (1H, ddt, 13.7, 6.9, 1.2 Hz), 1.13 (d, 3H, $J$ = 6.8 Hz). To the best of our knowledge, the $^1$H NMR data of this known compound have never been reported.[33]

**(±)-2-Fluoro-2,3-epoxynerol ((±)-2).** Compound (±)-**2** was prepared by Sharpless's vanadium-catalyzed *tert*-butyl hydroperoxide epoxidation with modifications. Representative procedure: to a stirring solution of 2-fluoronerol[11] (112 mg, 0.65 mmol) in dry $CH_2Cl_2$ (8 mL) were added vanadyl(IV) acetylacetonate ($VO(acac)_2$, 25 mg, 0.094 mmol) and *tert*-butyl hydroperoxide (TBHP, 5−6 M in decane, 168.0 μL, 0.84−1.00 mmol). After 35 min at room temperature, the reaction was quenched by addition of 5% aqueous NaOH (4 mL). The mixture was extracted with $Et_2O$ (3 × 5 mL), the combined extracts were dried over $MgSO_4$, and the solvent was removed under reduced pressure. Purification by flash chromatography on silica gel (previously washed with 10% triethylamine/$Et_2O$) using 10% EtOAc−hexane as eluent yielded (±)-**2** (118.1 mg, 96%) as a colorless oil: $R_f$ 0.23 (10% $Et_2O$−pentane); $^1$H NMR (400 MHz, $C_6D_6$) δ 5.01 (1H, tq, $J$ = 6.8, 1.2 Hz, H-6), 3.78 (1H, dt, $J$ = 12.5, 5.2 Hz, H-1), 3.59 (1H, ddd, $^3J_{H-F}$ = 22.2 Hz, and $J$ = 12.5, 6.8 Hz, H-1), 1.99 (2H, m, H-5), 1.67 (1H, t, $J$ = 6.2 Hz), 1.60 (3H, s, Me-7), 1.47 (3H, s, Me-7), 1.34 (1H, ddd, $J$ = 14.2, 9.6, 7.1 Hz) 1.33 (3H, s, Me-3); $^1$H NMR (500 MHz, $CDCl_3$) δ 5.09 (1H, tt, $J$ = 7.5, 1.5 Hz, H-6), 4.05 (1H, dt, $J$ = 13.0, 6.0 Hz, H-1), 3.88 (1H, ddd, $^3J_{H-F}$ = 20.5 Hz, and $J$ = 13.0, 7.5 Hz, H-1), 2.15 (2H, app q, $J$ = 7.8, H-5), 1.81 (1H, t, $J$ = 7.0 Hz), 1.70 (3H, s, Me-7), 1.63 (3H, s, Me-7), 1.52 (1H, dt, $J$ = 14.0, 8.5 Hz) 1.49 (3H, s, Me-3); $^{13}$C NMR (100 MHz, $C_6D_6$) 132.4, 123.4, 100.0 (d, $J$ = 264 Hz), 67.0 (d, $J$ = 19.0 Hz), 60.8 (d, $J$ = 25.7 Hz), 33.7 (d, $J$ = 2.3 Hz), 25.7, 23.9, (d, $J$ = 1.5 Hz), 17.5, 16.6; $^{19}$F NMR (376 MHz, $C_6D_6$) δ −143.88 (dd, $J$ = 21.5, 10.5 Hz); IR (film): 3381, 1664, 1379, 1266, 1148, 1016; LR(CI)MS $m/z$ (rel int): 189 [$M^+$ + 1] (3), 169 (12), 151 (25), 133 (16), 123 (53), 109 (52), 101 (31), 93 (31), 81 (20), 69 (100); LRMS (EI) $m/z$ (rel int) 168 (12), 149 (8), 137 (16), 109 (45), 95 (31), 82 (16), 69 (100); HRMS (EI-TOF) $m/z$ [$M^+$ + H] calcd for $C_{10}H_{18}FO_2$ 189.1291, found 189.1288.

**(±)-2-Fluoro-2,3-epoxygeraniol.** Epoxidation of 2-fluorogeraniol[11] (50 mg, 0.29 mmol) as described for (±)-**2** gave the title compound (52 mg, 94%) as a colorless oil: $^1$H NMR (500 MHz, $CDCl_3$) δ 5.12 (1H, tt, $J$ = 7.2, 1.3 Hz, H-6), 4.08 (1H, dt, $J$ = 12.6, 5.9 Hz, H-1), 3.88 (1H, ddd, $^3J_{H-F}$ = 20.5 Hz, $J$ = 13.1, 7.6 Hz, H-1), 2.16 (2H, app q, $J$ = 7.6, H-5), 1.89−1.79 (1H, m), 1.76−1.71 (1H, m), 1.69 (3H, broad d, $J$ = 1.2 Hz, Me-7), 1.62 (3H, s, Me-7), 1.38 (3H, d, $J$ = 2.3 Hz, Me-3); $^{13}$C NMR (125 MHz, $CDCl_3$) 132.5, 122.9, 100.6 (d, $J$ = 265 Hz), 67.4 (d, $J$ = 18.9 Hz), 60.9 (d, $J$ = 36.5 Hz), 32.8, 25.6, 23.6, 17.6, 17.1; $^{19}$F NMR (282 MHz, $CDCl_3$) δ −144.99 (dd, $J$ = 22.2, 13.8 Hz); IR (film) 3392, 1647, 1377, 1267, 1147, 1020; LRMS (EI) $m/z$ (rel int) 168 (12), 150 (8), 137 (18), 125 (10), 109 (65), 95 (30), 82 (70), 67 (100), 69 (80), 55 (65); HRMS (EI-TOF) $m/z$ [$M$ − HF]$^+$ calcd for $C_{10}H_{16}O_2$ 168.1150, found 168.1146; HRMS (CI-TOF) $m/z$ [$M$ + H]$^+$ calcd for $C_{10}H_{18}FO_2$ 189.1291, found 189.1262.

**(±)-2-Fluoro-2,3-epoxyneryl Acetate ((±)-3).** To a solution of (±)-**2** (20 mg, 0.11 mmol) in $CH_2Cl_2$ (0.5 mL) were added pyridine (200 μL, 195.6 mg, 2.48 mmol) and acetic anhydride (50 μL, 54 mg, 0.53 mmol) at room temperature. After 12 h, the solvents were evaporated using a stream of nitrogen, and the residue was purified by preparative TLC on silica gel (previously treated with 10% triethylamine−$Et_2O$ and dried at room temperature) using 5% $Et_2O$−pentane as eluent to yield pure acetate (±)-**3** (22 mg, 89%) as a colorless oil: $R_f$ 0.46 (10% $Et_2O$-pentane); $^1$H NMR (500 MHz, $C_6D_6$) δ 4.99 (1H, t, $J$ = 1.5 Hz, H-6), 4.44 (1H, dd, $^3J_{H-F}$ = 15.3 Hz, and $J$ = 12.8, Hz, H-1), 4.27 (1H, dd, $^3J_{H-F}$ = 19.9 Hz, and $J$ = 12.8, Hz, H-1), 1.97 (2H, m, H-5), 1.60 (6H, s, Me-7 and Ac), 1.50−1.44 (1H, m), 1.45 (3H, s, Me-7), 1.36−1.32 (1H, m), 1.29 (3H, d, $J$ = 1.0 Hz, Me-3); $^{13}$C NMR (100 MHz, $C_6D_6$) 169.5, 132.5, 123.2, 99.0 (d, $J$ = 264 Hz), 67.0 (d, $J$ = 19.0 Hz), 61.3 (d, $J$ = 33.4 Hz), 33.7, 25.7, 23.7, 19.9, 17.5, 16.3; $^{19}$F NMR (376 MHz, $C_6D_6$) δ −141.64 (t, $J$ = 16.5 Hz); IR (film): 1745, 1639, 1378, 1268, 1234, 1154, 1047; HRMS (EI-TOF) $m/z$ [$M$]$^+$ calcd for $C_{12}H_{19}FO_3$ 230.1318, found 230.1316.

(±)-2-Fluoro-2,3-epoxyneryl [1-$^{13}$C,$^{18}$O]-acetate ($^{13}$C, $^{18}$O-**3**) was prepared by carbodiimide esterification of (±)-**2** using [1-$^{13}$C,$^{18}$O]-acetic acid, the latter prepared from [$^{18}$O]-$H_2O$ (95%) and [1-$^{13}$C]-acetic acid (99%).[22c]

**(±)-2-Fluoro-2,3-epoxygeranyl Acetate.** By acetylation ($Ac_2O$/Py, 93%) of (±)-2-fluoro-2,3-epoxygeraniol (25 mg, 0.13 mmol) as described for (±)-**3**: $^1$H NMR (400 MHz, $C_6D_6$) δ 5.09 (1H, app tt, $J_{app}$ = 7.2, 1.3 Hz, H-6), 4.35 (1H, dd, $^3J_{H-F}$ = 13.4 Hz, and $J$ = 12.6 Hz, H-1), 4.21 (1H, dd, $^3J_{H-F}$ = 21.3 Hz, and $J$ = 12.6 Hz, H-1), 2.08 (2H, app q, $J_{app}$ = 7.7 Hz, H-5), 1.87−1.66 (2H, m), 1.60 (3H, d, $J$ = 1.5 Hz, Me-7), 1.59 (3H, s, Ac), 1.48 (3H, s, Me-7), 1.03 (3H, d, $J$ = 2.6 Hz, Me-3); $^{13}$C NMR (125 MHz, $C_6D_6$) 169.5, 132.2, 123.2, 99.0 (d, $J$ = 264 Hz), 67.0 (d, $J$ = 18.1 Hz), 61.4 (d, $J$ = 32.8 Hz), 32.9, 25.7, 24.0, 19.9, 17.5, 17.0; $^{19}$F NMR (282 MHz, $CDCl_3$) δ −143.1 (t, $J$ = 15.8 Hz); IR (film): 1749, 1630, 1377, 1265, 1234, 1155, 1048; HRMS (EI-TOF) $m/z$ [$M$]$^+$ calcd for $C_{12}H_{19}FO_3$ 230.1318, found 230.1313.

**((2*R*,3*R*)-2-Fluoro-3-methyl-3-(4-methylpent-3-en-1-yl)-oxiran-2-yl)methanol [(2*R*,3*R*)-2-Fluoro-2,3-epoxynerol] (2).** Compound **2** was prepared by Sharpless's titanium-catalyzed asymmetric *tert*-butyl hydroperoxide epoxidation.[23] To a cold (−20 °C) solution of L-(+)-diethyl tartrate (82 mg, 0.40 mmol) in dry $CH_2Cl_2$ (4 mL) were successively added titanium(IV) isopropoxide (113 mg, 0.40 mmol) and a solution of 2-fluoronerol (69 mg, 0.4 mmol) in $CH_2Cl_2$ (1 mL) under $N_2$. After 15 min of stirring at this temperature, *tert*-butyl hydroperoxide (5−6 M in decane, 160−133 μL, 0.8 mmol) was added. The resulting mixture was kept at −20 °C for 22 h and worked up as described by Katsuki and Sharpless[23] to give, after silica gel chromatography using a gradient of 10−20% EtOAc−hexane as eluent, 57 mg of a 7:3 mixture of (2*R*,3*R*)-2-fluoro-2,3-epoxynerol (**2**) and unreacted starting material. Further elution of the column with $Et_2O$ afforded 9.2 mg (12%) of pure 1,3-dihydroxy-3,7-dimethyl-6-octen-2-one (**1**).[5] Repurification of the mixture by silica gel chromatography using 5% EtOAc−hexane gave starting 2-fluoronerol (14 mg, 20%) and **2** (40 mg, 54%). Analysis of this material by chiral GC[5,9] ($t_R$ = 20.80 min (major, 83.4%) and 21.14 min (minor, 16.6%)


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revealed an ee of 68%. Repetition of Sharpless's asymmetric epoxidation at lower temp (−40, and −60 °C) for extended reaction times (48 h) gave **2** with an enantiomeric excess of 91%, and 85% ee, respectively, and improved reaction yields of 86−89%. Thus, to a cold (−40 °C or −60 °C) and stirred solution of L-(+)-diethyl tartrate (344 μL, 414.2 mg, 2.0 mmol) in $CH_2Cl_2$ (8 mL) were successively added titanium(IV) isopropoxide (592 μL, 568.3 mg, 2.0 mmol) and a solution of 2-fluoronerol (290 mg, 1.68 mmol) in dry $CH_2Cl_2$ (3 mL) under $N_2$. After 15 min of stirring at this temperature, *tert*-butyl hydroperoxide (5−6 M in decane, 664 μL, 3.32−3.98 mmol) was added. The resulting mixture was kept at −40 °C (or −60 °C) for 48 h and worked up exactly as described by Katsuki and Sharpless[23] to give, after purification by "deactivated" silica gel chromatography using 5% EtOAc−hexane as eluent, pure (2*R*,3*R*)-2-fluoro-2,3-epoxynerol (**2**, −40 °C, 278 mg, 88% yield, 91% ee, or **2**, −60 °C, 272 mg, 86% yield, 85% ee) as evidenced by chiral GC. The $^1H$, $^{13}C$, and $^{19}F$ NMR spectra and data of these materials were identical to those previously described for racemic 2-fluoro-2,3-epoxynerol (±)-**2**.

**((2*S*,3*R*)-2-Fluoro-3-methyl-3-(4-methylpent-3-en-1-yl)-oxiran-2-yl)methanol [(2*S*,3*R*)-2-Fluoro-2,3-epoxygeraniol] ((2*S*,3*R*)-2).** Compound (2*S*,3*R*)-**2** was prepared by Sharpless asymmetric epoxidation (−20 °C) of 2-fluorogeraniol (60 mg, 0.35 mmol) as described above for **2**, using in this case D-(−)-diethyl tartrate. Chiral GC analysis of the product (58 mg, 88% yield) revealed an ee of 70%. The $^1H$, $^{13}C$, and $^{19}F$ NMR spectra and data were identical to those described above for racemic 2-fluoro-2,3-epoxygeraniol.

**((2*R*,3*R*)-2-Fluoro-3-methyl-3-(4-methylpent-3-en-1-yl)-oxiran-2-yl)methyl Acetate [(2*R*,3*R*)-2-Fluoro-2.3-epoxyneryl Acetate] (3).** Acetylation of chiral 2-fluoro-2,3-epoxynerol (**2**, 40 mg, 0.21 mmol, 68% ee, **2**, 30 mg, 0.16 mmol, 91% ee, and **2**, 188 mg, 1.00 mmol, 85% ee) as described for (±)-**3** afforded chiral epoxy acetates (**3** 46 mg, 93%, **3**, 32 mg, 86%, and **3**, 213 mg, 93%), respectively. The $^1H$, $^{13}C$, and $^{19}F$ NMR spectra and data of these materials were identical to those previously obtained for (±)-**3**.

**((2*S*,3*R*)-2-Fluoro-3-methyl-3-(4-methylpent-3-en-1-yl)-oxiran-2-yl)methyl acetate [(2*S*,3*R*)-2-fluoro-2,3-epoxygeranyl Acetate] ((2*S*,3*R*)-3).** Acetylation of (2*S*,3*R*)-**2** (53 mg, 0.28 mmol, 70% ee), as described for (±)-**3**, afforded (2*S*,3*R*)-**3** (62 mg, 96%). The $^1H$, $^{13}C$, and $^{19}F$ NMR spectra and data of the product were identical to those described above for racemic 2-fluoro-2,3-epoxygeraniol acetate.

**(*S*)-3-Hydroxy-3,7-dimethyl-2-oxooct-6-en-1-yl Acetate (5) and (*S*)-1-Hydroxy-3,7-dimethyl-2-oxooct-6-en-3-yl Acetate (6).** *A. By Acid-Catalyzed Hydrolysis of (2R,3R)-2-Fluoro-2,3-epoxyneryl Acetate (3) or (2S,3R)-3 in Solution.* Representative procedure: To a solution of **3** (100 mg, 440 μmol, 91% ee) in 0.3% water−benzene (7 mL) was added a 0.6 M solution of trifluoroacetic acid in benzene (50 μL, 30 μmol). After 48 h at room temperature, triethylamine (100 μL, 723 μmol) was added, and the resulting mixture was evaporated with a stream of nitrogen. Purification by silica gel chromatography using 50% EtOAc−hexanes afforded a 3:2 mixture of primary (**5**) and secondary (**6**) acetates (92.2 mg, 92%). The same procedure was repeated with **3** (106 mg, 450 μmol, 68% ee), **3** (180 mg, 780 μmol, 85%), and (2*S*,3*R*)-**3** (36 mg, 0.16 mmol) to give a similar 3:2 mixture of **5** and **6** in 92, 89%, and 90% yield, respectively.

For kinetic measurements, the same reaction was run in an NMR tube using (2*R*,3*R*)-2-fluoro-2,3-epoxynerol acetate (**3**, 18 mg, 78 μmol, 85% ee) in 0.2% $D_2O$−$C_6D_6$ (0.7 mL). The reaction was initialized by the addition of trifluoroacetic acid (0.6 M in $C_6D_6$, 20 μL, 12 μmol), and the progress of the reaction was monitored ($^1H$ and $^{19}F$ NMR) by the gradual disappearance of the characteristic NMR peaks of **3** at $\delta_H$ 4.44 (1H, dd, $J$ = 15.3, 12.8, Hz, H-1) and 4.27 (1H, dd, $J$ = 19.9, 12.8, Hz, H-1), or $\delta_F$ −141.64 (t, $J$ = 16.5 Hz). The estimated half-life ($t_{1/2}$) for this experiment was 5 h. After 26 h, $^1H$ NMR analysis (500 MHz) showed the total disappearance of **3**, and a 2:1 mixture of **5** and **6** (16 mg, 90%) was obtained after workup.

*B. By Acid-Catalyzed Hydrolysis of (2R,3R)-2-Fluoro-2,3-epoxyneryl Acetate (3) Using Silica Gel.* A solution of **3** (12 mg, 52 μmol, 85% ee) in dry $CH_2Cl_2$ (0.5 mL) was applied to a preparative TLC (silica) plate. After 0.5 h, the plate was developed using 40% $Et_2O$-hexanes to give, after elution with dry $Et_2O$ and evaporation of solvent with a stream of $N_2$, a 1:2 mixture of primary (**5**) and tertiary (**6**) acetates (10 mg, 84%). For characterization purposes this material was further purified by preparative TLC on silica gel (15% $Et_2O$−hexanes, three developments) to give pure samples of acetates **5** and **6**.

**Data for (*S*)-3-hydroxy-3,7-dimethyl-2-oxooct-6-en-1-yl acetate (5):** colorless oil; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 5.07 (app tq, $J_{app}$ = 7.3, 1.5 Hz, 1H, H6), 4.98 (d, $J$ = 17.5 Hz, 1H, H1a), 4.94 (d, $J$ = 17.5 Hz, 1H, H1b), 3.03 (s, 1H, OH), 2.18 (s, 3H), 2.09 (m, 1H), 1.96 (m, 1H), 1.81 (ddd, $J$ = 14.2, 10.2, 5.9 Hz, 1H), 1.71 (ddd, $J$ = 14.2, 10.2, 5.9 Hz, 1H), 1.67 (s, 3H), 1.60 (s, 3H), 1.39 (s, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 207.4, 170.3, 133.2, 123.1, 78.8, 64.9, 39.7, 25.9, 25.7, 22.1, 20.5, 17.7; LRMS (CI) $m/z$ (rel int) 227 $[M - H]^+$ (8), 211 (13), 169 (28), 151 (100), 143 (31), 133 (31), 123 (38), 109 (39), 93 (26), 83 (12), 69 (64); IR (film) 3497, 1753, 1727, 1374, 1262, 1232, 1040; HRMS (CI-TOF) $m/z$ $[M - H]^+$ calcd for $C_{12}H_{19}O_4$ 227.1283, found 227.1285.

**Data for (*S*)-1-hydroxy-3,7-dimethyl-2-oxooct-6-en-3-yl acetate (6):** colorless oil; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 5.02 (tt, $J$ = 7.1, 1.5 Hz, 1H, H6), 4.42 (dd, $J$ = 19.1, 4.9 Hz, 1H, H1a), 4.34 (dd, $J$ = 19.1, 4.9 Hz, 1H, H1b), 2.98 (t, $J$ = 4.9 Hz, 1H, OH), 2.09 (s, 3H), 2.01−1.89 (m, 3H), 1.84 (ddd, $J$ = 13.7, 10.2, 5.9 Hz, 1H), 1.67 (s, 3H), 1.58 (s, 3H), 1.57 (s, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 208.9, 170.8, 133.0, 122.5, 84.7, 64.7, 37.0, 25.7, 21.8, 21.2, 20.7, 17.6; IR (film): 3438, 1750, 1729, 1715, 1373, 1268, 1238, 1023; LRMS (CI) $m/z$ (rel int) 227 $[M - H]^+$ (4), 211 (4), 169 (14), 151 (26), 133 (8), 123 (25), 111 (26), 101 (27), 93 (18), 86 (70), 84 (100), 69 (56); LRMS (EI) $m/z$ (rel int) 168 $[M - AcOH]^+$ (6), 146 (6), 109 (18), 93 (18), 86 (64), 84 (100), 69 (16); HRMS (CI-TOF) $m/z$ $[M - H]^+$ calcd for $C_{12}H_{19}O_4$ 227.1283, found 227.1282.

**(*S*)-1,3-Dihydroxy-3,7-dimethyl-6-octen-2-one ((*S*)-CPB Pheromone, 1).** Representative procedure: A suspension of a 3:2 mixture of acetates **5** and **6** (15 mg, 0.07 mmol), obtained from epoxy alcohol **2** (85% ee), was stirred in MeOH (1 mL) containing $K_2CO_3$ (40 mg, 0.29 mmol) for 1 h at rt. Water (2 mL) was added, and the resulting solution was neutralized with 10% aqueous HCl. The mixture was extracted with $Et_2O$ (3 × 3 mL), the organic layer was dried ($MgSO_4$) and the solvent evaporated with a stream of $N_2$. Purification by preparative TLC on silica gel (50% EtOAc−hexene) gave the pure product (11 mg, 90%) as a colorless oil. Chiral CG analysis of this material revealed an enantiomeric excess of 87% ee. This procedure was repeated with a 5:3 mixture of (**5** + **6**) (9 mg, 0.04 mmol) obtained from epoxy alcohol **2** (68% ee) and a 3:2 mixture of (**5** + **6**) (9 mg, 0.04 mmol) obtained from epoxy alcohol **2** (91% ee) to give the corresponding diol **1** in 91−93% yields with a measured (chiral GC) enantiomeric excesses of 72% and 96% ee, respectively. The reason for the observed 4−5% increase in ee is unknown.

**Data for the (*S*)-CPB pheromone (1).** The material obtained with 96% ee has: $[\alpha]^{25}_D$ = +3.2 (*c* 0.4, $CHCl_3$) [lit.[9] +3.8 (*c* 0.89, $CHCl_3$)]; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 5.02 (t quintet, $J$ = 7.2, 1.5 Hz, 1H, H6), 4.52 (dd, $J$ = 19.8, 4.9 Hz, 1H, H1a), 4.46 (dd, $J$ = 19.8, 0.4.9 Hz, 1H, H1b), 2.94 (t, $J$ = 4.9 Hz, 1H, 1-OH), 2.93 (s, 1H, 3-OH), 2.08 (app sextet $J_{app}$ = 7.2 Hz, 1H), 1.90 (app sextet $J_{app}$ = 7.2 Hz, 1H), 1.79 (ddd, $J$ = 14.1, 10.1, 6.1 Hz, 1H), 1.71 (ddd, $J$ = 14.1, 10.0, 5.9 Hz, 1H), 1.66 (s, 3H), 1.58 (s, 3H), 1.37 (s, 3H). The $^1H$ NMR spectrum was superimposable to that obtained from silica gel treatment of **2** (see above). In addition, the $^1H$ NMR data are in total agreement with those previously published for the (*S*)-CPB pheromone at 500 MHz.[9]

**(1*R*,5*S*,8*S*)-8-(2-Fluoropropan-2-yl)-1,5-dimethyl-2,9-dioxabicyclo[3.3.1]nonan-4-one (8) and (1*R*,5*S*,8*R*)-1,5-Dimethyl-8-(prop-1-en-2-yl)-2,9-dioxabicyclo[3.3.1]nonan-4-one (9).** Trifluoroacetic acid (0.6 M in anhydr $C_6D_6$, 10 μL, 6 μmol) was added to an oven-dried NMR tube containing a solution of **3** (27 mg, 0.12 mmol, 85% ee) in $C_6D_6$ (0.7 mL) at rt. This material contained 14% of 2-fluoronerol acetate (0.0177 mmol) which was used as an internal standard. The progress of the reaction was monitored by $^1H$ and $^{19}F$ NMR spectroscopy. After 24 h, the reaction was worked up by evaporation of the solvent with a stream of $N_2$. Purification of the residue by preparative TLC on silica gel (5% $Et_2O$−hexane) gave


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fluorinated bicyclic ketal **8** (23 mg, 85%) and small amounts of olefin **9** (ca. 2 mg, 8%). When the reaction was carried out in dry $CD_3CN$ (0.7 mL) starting from **3** (25 mg, 0.11 mmol), a total of 30 $\mu$L of the 0.6 M TFA solution was required to initiate the reaction. As evidenced by $^{19}F$ NMR spectroscopy (376 MHz), the reaction was slower than that in $C_6D_6$, with an estimated conversion of 85% after 26 h at room temp. After 48 h, the reaction was worked up as described above to give, after purification by preparative TLC **8** (6 mg, 25%), **9** (12 mg, 52%), and the hydrolysis product **5** (4 mg, 17%).

**Data for 8:** colorless oil; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 4.38 (d, $J$ = 14.2 Hz, 1H), 3.81 (d, $J$ = 14.2 Hz, 1H), 2.01 (app dd, $J_{app}$ = 13.2, 3.0 Hz, 1H), 1.93 (dt, $J$ = 11.2, 4.5 Hz, 1H), 1.58−1.50 (m, 3H), 1.53 (d, $^5J_{H-F}$ = 4.4 Hz, 3H), 1.35 (d, $^3J_{H-F}$ = 22.2 Hz, 3H), 1.32 (d, $^3J_{H-F}$ = 22.2 Hz, 3H), 1.26 (s, 3H); $^{13}C$ NMR (151 MHz, $CDCl_3$) $\delta$ 213.0 (s) (d, $J_{C-F}$ = 0.7 Hz), 100.6 (s) (d, $J_{C-F}$ = 1.3 Hz), 97.5 (s) (d, $J_{C-F}$ = 165.9 Hz), 80.6 (s), 65.4 (t), 53.1 (d) (d, $J_{C-F}$ = 21.1 Hz), 34.0 (t) (d, $J_{C-F}$ = 1.0 Hz), 28.4 (q) (d, $J_{C-F}$ = 25.4 Hz), 25.4 (q) (d, $J_{C-F}$ = 7.6 Hz), 23.9 (q), 23.7 (q) (d, $J_{C-F}$ = 24.5 Hz), 20.9 (t) (d, $J_{C-F}$ = 9.6 Hz); $^{19}F$ NMR $\delta_F$ −127.44 (br s); IR (film) 1743, 1375, 1266, 1224, 1199, 1148, 1119, 1079, 1047, 973, 916, 868, 798, 738, 704; LRMS (EI) $m/z$ (rel int) 230 $[M]^+$ (6), 210 (6), 199 (5), 182 (6), 171 (42), 139 (20), 126 (30), 111 (100), 100 (55), 73 (70), 69 (95); HRMS (EI-TOF) $m/z$ $[M]^+$ calcd for $C_{12}H_{19}FO_3$ 230.1318, found 230.1317.

**Data for 9:** colorless oil; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta_H$ 4.85 (br s, 2H), 4.39 (d, $J$ = 14.4 Hz, 1H), 3.88 (d, $J$ = 14.4 Hz, 1H), 2.28 (dd, $J$ = 12.7, 3.7 Hz, 1H), 2.01 (ddd, $J$ = 13.4, 4.4, 2.5 Hz, 1H), 1.85 (dq, $J$ = 13.4, 4.4 Hz, 1H), 1.73 (s, 3H), 1.57 (dt, $J$ = 13.7, 4.9 Hz, 1H), 1.48 (dm, $J$ = 13.7 Hz, 1H), 1.38 (s, 3H), 1.29 (s, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 215.8 (s), 145.4 (s) 114.3 (t), 100.3 (s), 80.9 (s), 65.7 (t), 52.3 (d), 33.7 (t), 24.1 (q), 23.8 (q), 23.2 (t), 20.9 (q); LRMS (EI) $m/z$ (rel int) 210 $[M]^+$ (4), 197 (5), 168 (4), 150 (8), 137 (12), 109 (26), 68 (100); HRMS (EI-TOF) $m/z$ $[M]^+$ calcd for $C_{12}H_{18}O_3$ 210.1256, found 210.1258.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

Reproduction of 1D, 2D NMR spectra, GC chromatograms, and spectra of kinetic runs followed by $^1H$, $^{13}C$, and $^{19}F$-NMR spectroscopy. This material is available free of charge via the Internet at http://pubs.acs.org

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### Notes

The authors declare no competing financial interest.

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## ■ DEDICATION

In memory of Robert Milton Silverstein (1917−2007), pioneer of insect pheromone chemistry and organic spectrometry.

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