until the solution became colorless. Methyl sulfide (3.0 mL) was added, and the mixture was warmed to 25 °C. The mixture was stirred for 2 h (orange-red color reappeared), and the solvent was evaporated to furnish the crude diastereomeric lactols, which were oxidized directly.

To a suspension of pyridinium chlorochromate (4.4 g, 20.4 mmol), powdered 4-Å molecular sieves (10 g), and anhydrous NaOAc (300 mg) in CH_2Cl_2 (50 mL) was added a solution of the crude lactols in CH_2Cl_2 (5 mL). The reaction mixture was stirred at 25 °C for 3 h, and then the mixture was poured onto a column of silica gel (150 g). The column was eluted with 50% EtOAc–petroleum ether to give a 1:1 mixture of spiro lactams **14a** and **14b** (3.11 g). The spiro lactams were dissolved in 5% Et_2O–petroleum ether (10–15 mL) and stored at 4 °C overnight. A white solid (R_f 0.35, 30% EtOAc–petroleum ether) was obtained and collected by filtration. Recrystallization (Et_2O–petroleum ether) of the material gave lactone **14a** (880 mg, 21%) as white needles. For **14a**: mp 138–139 °C; R_f 0.35 (silica gel, 30% EtOAc–petroleum ether); $[\alpha]^{25}_D$ −22.8° (*c* 1.15, $CHCl_3$); IR (Nujol) 2920, 1750, 1730, 1710, 1460, 1370 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (br s, 5 H, Ar), 5.50 (br d, 1 H), 5.10 (s, 2 H), 5.05 (m, 1 H), 3.55 (d, 1 H, *J* = 7.0 Hz), 3.35 (d, 1 H, *J* = 7.0 Hz), 2.70 (m, 1 H), 2.30 (m, 2 H), 1.75 (m, 1 H), 0.95 (s, 9 H), 0.25 (s, 6 H); ^{13}C NMR (CD_3OD) δ 179.2 (q), 174.3 (q), 158.6 (q), 138.2 (q), 129.5 (s), 129.2 (s), 128.8 (s), 86.0 (q), 67.7 (d), 55.5 (s), 54.3 (d), 32.5 (d), 27.1 (d), 26.4 (t), 19.4 (q), −6.1 (t); mass spectrum, *m/e* 419 (M + H). Anal. Calcd for $C_{21}H_{30}N_2O_5Si$: C, 60.26; H, 7.22; N, 6.69. Found: C, 60.34; H, 7.20; N, 6.58.

The filtrate was concentrated and repeatedly purified by chromatography (50% EtOAc–petroleum ether) to provide diastereomer **14b** (1.0 g, 23%). An analytical sample of **14b** was obtained upon recrystallization from Et_2O–petroleum ether. For **14b**: mp 121–122 °C; R_f 0.40 (silica gel, 30% EtOAc–petroleum ether); $[\alpha]^{25}_D$ +52.3° (*c* 0.65, $CHCl_3$); IR (Nujol) 2920, 1745, 1710, 1460, 1370 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (s, 5 H, Ar), 5.70 (d, 1 H, *J* = 8.5 Hz), 5.10 (s, 2 H), 4.35 (m, 1 H), 3.45 (dd, 2 H, *J* = 16.5, 7.0 Hz), 2.50–2.00 (m, 4 H), 0.95 (s, 9 H), 0.25 (s, 3 H), 0.22 (s, 3 H); ^{13}C NMR (CD_3OD) δ 179.8 (q), 175.3 (q), 158.6 (q), 138.1 (q), 129.5 (s), 129.0 (s), 128.8 (s), 85.7 (q), 68.1 (d), 55.4 (s), 54.4 (d), 32.3 (d), 27.2 (d), 26.3 (t), 19.4 (q), −6.1 (t); mass spectrum, *m/e* 418 (M^+), 261, 233, 91. Anal. Calcd for $C_{21}H_{30}N_2O_5Si$: C, 60.26; H, 7.22; N, 6.69. Found: C, 60.30; H, 7.07; N, 6.55.

(3*S*,3′*S*)-3-[3′-[(Benzyloxycarbonyl)amino]-3′-carboxypropyl]-3-hydroxy-2-oxoazetidine δ-Lactone (15a) and the 3*R*,3′*S* Diastereomer (15b). A solution of lactone **14a** (660 mg, 1.60 mmol) in THF (3 mL) containing glacial acetic acid (0.3 mL, 5.0 mmol) was treated with *n*-Bu_4NF (1.9 mL of a 1 M THF solution, 1.9 mmol). The mixture was stirred for 1 h, and then solvents were removed in vacuo. Purification of the residue by chromatography (1% MeOH–EtOAc) gave lactone **15a** (405 mg, 84%): foam; R_f 0.50 (EtOAc); IR (Nujol) 1745, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (s, 5 H), 5.90 (br s, 1 H), 5.55 (br s, 1 H), 5.10 (s, 2 H), 5.00 (m, 1 H), 3.70 (d, 1 H, *J* = 7.0 Hz), 3.45 (d, 1 H, *J* = 7.0 Hz), 2.70 (m, 1 H), 2.35 (m, 2 H), 1.80 (m, 1 H); mass spectrum, *m/e* 305 (M + H), 261, 91; high-resolution FAB mass spectrum calcd for $C_{15}H_{16}N_2O_5$ 304.2790, found 304.2780.

Lactone **15b** was prepared by analogous desilylation of intermediate lactone **14b**. For **15b**: foam; R_f 0.5 (EtOAc); IR (Nujol) 1745, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (s, 5 H), 6.10 (br s, 1 H), 5.62 (d, 1 H, *J* = 8.5 Hz), 5.10 (s, 2 H), 4.35 (m, 1 H), 3.55 (m, 2 H), 2.60–2.05 (m, 4 H); mass spectrum, *m/e* 305 (M + H); high-resolution FAB mass spectrum calcd for $C_{15}H_{16}N_2O_5$ 304.2790, found 304.2775.

(3*S*,3′*S*)-3-(3′-Amino-3′-carboxypropyl)-3-hydroxy-2-oxoazetidine (Tabtoxinine β-Lactam) (1) and the 3*R*,3′*S* Diastereomer (17). To a solution of spiro lactam **15a** (760 mg, 2.5 mmol) in THF–H_2O (3:1, 20 mL) was added 1 N aqueous NaOH (3 mL, 3.0 mmol). The solution was stirred at 25 °C for 30 min and then neutralized with an acidic ion-exchange resin (Dowex 50W×2, 100–200 mesh, Biorad). The suspension was filtered, and the solvents were evaporated in vacuo. The residue was dissolved in a small portion of water and lyophilized to yield *N*-Cbz protected tabtoxinine β-lactam **16a** (590 mg, 75%) as a white powder. The remaining material (25%) was not recovered from the resin.

Acid **16a** so obtained was dissolved in water (40 mL) to which 10% Pd/C (40 mg) was added. The suspension was stirred under ambient H_2 pressure for 2 h. The reaction mixture was filtered and the filtrate lyophilized to afford analytically pure tabtoxinine β-lactam **1** (38 mg, 100% foam **16a**): amorphous white solid; R_f 0.35 (silica gel, 2:1:1 *n*-BuOH–HOAc–H_2O); $[\alpha]^{25}_D$ −23.7° (*c* 0.30, H_2O); IR (KBr) 3420, 3250, 1745, 1630 cm^{-1}; ^1H NMR (D_2O) δ 3.75 (m, 1 H), 3.50 (d, 1 H, *J* = 7.0 Hz), 3.35 (d, 1 H, *J* = 7.0 Hz), 2.20–1.70 (m, 4 H); ^{13}C NMR (D_2O) δ 181.8 (q), 176.5 (q), 72.7 (q), 59.8 (s), 49.5 (d), 33.2 (d), 25.5 (d); mass spectrum, *m/e* 189 (M + H). Anal. Calcd for $C_7H_{12}N_2O_4$: C, 76.58; H, 6.42; N, 14.88. Found: C, 76.50; H, 6.40; N, 14.52.

The corresponding 3*R*,3′*S* diastereomer **17** was obtained in analogous fashion from **15b** via intermediate **16b**. For **17**: amorphous white solid; R_f 0.35 (silica gel, 2:1:1 *n*-BuOH–HOAc–H_2O); $[\alpha]^{25}_D$ +35.0° (*c* 0.22, H_2O); IR (Nujol) 3340, 1720, 1620 cm^{-1}; ^1H NMR (D_2O) δ 3.80 (m, 1 H), 3.50 (d, 1 H, *J* = 7.0 Hz), 3.35 (d, 1 H, *J* = 7.0 Hz), 2.20–1.80 (m, 4 H); ^{13}C NMR (D_2O) δ 181.8 (q), 176.3 (q), 72.1 (q), 60.1 (s), 49.6 (d), 34.4 (d), 25.6 (d); mass spectrum, *m/e* 189 (M + H). Anal. Calcd for $C_7H_{12}N_2O_4$: C, 76.58; H, 6.42; N, 14.88. Found: C, 76.48; H, 6.37; N, 14.89.

Supplementary Material Available: Experimental details of the X-ray structure determination of (−)-**14a**, ORTEP representation of (−)-**14a**, and tables of fractional atomic coordinates, thermal parameters, and interatomic distances and angles for (−)-**14a** (12 pages). Ordering information is given on any current masthead page.

Synthesis of Partially Fluorinated Analogues of (*Z*)-5-Decenyl Acetate: Probes for Hydrophobic Interaction in Pheromone Reception

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Selective regiochemical introduction of fluorines into methyl and methylene positions of (*Z*)-5-decenyl acetate provides analogues to probe the hydrophobicity requirements of the pheromone receptor site in the turnip moth, *Agrotis segetum*. Perfluorobutyl-, difluoromethylene-, trifluoromethyl-, and tetrafluoroethylene-containing analogues have been synthesized and chemically characterized.

Straight-chain monofunctionalized alkenes with a *Z* double bond constitute by far the largest class of known pheromone components produced by female moths (Insecta, Lepidoptera).[1] Each pheromone component is

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perceived by conspecific male moths using highly specialized receptor cells (sensilla) present in their antennae.[2] These sensilla can distinguish subtle chemical changes of a pheromonal molecule, such as the position or geometry of the double bond, as reflected by measurements of behavioral responses or of electrophysiological activity of single sensory cells. Large steric and electronic perturbations in structure often reduce biological activity by factors of 30–10 000.[3] Several models have been introduced to describe this structure–activity relationship based on electroantennogram (EAG) and field test results,[4] but these early models could not produce a satisfactory description of the pheromone–receptor interaction on a molecular level.[5]

A conformational energy model has been introduced by the Lund group[6] for the interaction between analogues of (*Z*)-5-decenyl acetate (*Z*5-10:Ac), the major sex pheromone component of the turnip moth *Agrotis segetum*,[7] and its receptor cells. The conformational energy model uses minimized energy values calculated by molecular mechanics to rationalize the electrophysiological activities measured by single sensillum recording technique. A strong correlation is obtained between calculated conformational energies required to mimic spatial relationships of *Z*5-10:Ac and the measured biological activities of analogues based on this pheromone component.

This model explains the effects of chain-elongation,[6a,b] change of double-bond configuration,[6b] the introduction of an additional *E* double bond at various positions,[8] and chain shortening[9] on the biological activities of *Z*5-10:Ac analogues. The terminal methyl group, the (*Z*)-alkene, and the acetoxy functionality all interact with complementary receptor sites in the receptor cavity. The terminal alkyl chain appears to interact with a hydrophobic "pocket" which includes the two methylene groups closest to the terminal methyl group. This result is consistent with previous findings that the terminal methyl group is important in pheromone activity[10] and further substantiates the importance of hydrophobicity of the terminal alkyl moiety in pheromone reception.

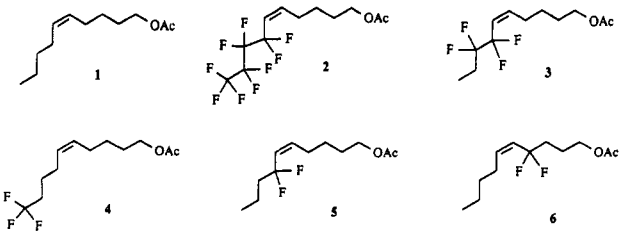

Figure 1. Structure of *Z*5-10:Ac (1) and fluorinated analogues.

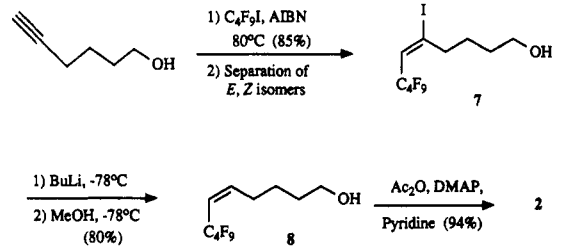

Figure 2. Synthesis of perfluorobutyl-*Z*5-10:Ac (2).

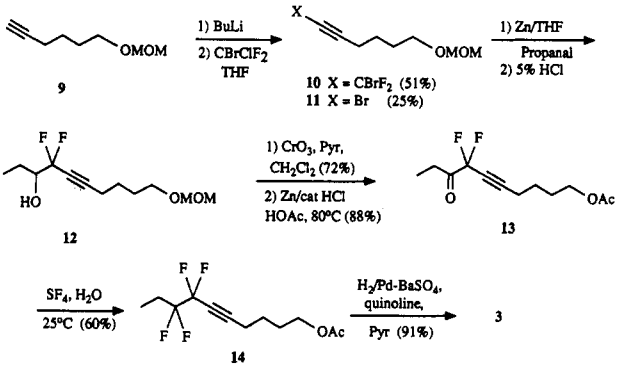

Figure 3. Synthesis of 7,7,8,8-tetrafluoro-*Z*5-10:Ac (3).

Perfluorinated moth pheromones[11] also support the importance of the hydrophobicity of the terminal alkyl group in pheromone–receptor protein interactions. Terminal butyl groups were replaced with perfluorobutyl groups, and male antennal olfactory receptor neurons from three moth species showed 100- to 10 000-fold lower activities relative to the parent compounds. In a study on the grape berry moth, partially-fluorinated analogues of the major pheromone component *Z*9-12:Ac were synthesized,[12] and unexpectedly varied behavioral responses were observed[13] for these analogues. Responses to the 11,11-difluoro analogues were indistinguishable from those to the natural pheromone, but the 12,12,12-trifluoromethyl analogue showed no attractancy. The 11,11,12,12,12-pentafluoro analogue was inactive when tested alone but synergized trap catches by the pheromone.

Biological responses of the oriental fruit moth, *Grapholita molesta*, to the allylic difluoromethylene pheromone analogues (*E*)- and (*Z*)-7,7-difluoro-8-dodecenyl acetate[14] suggest that the change in chemical reactivity

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(nucleophilicity) of the double bond caused by fluorine substitution plays little if any role in the interaction of the pheromone with its receptor. In contrast, the responses of the western spruce budworm, *Choristoneura occidentalis*, to a terminally monofluorinated pheromone analogue, 14F-*E*11-14:Al,[15] indicated a 14-fold shorter recovery period in EAG responses to the fluorinated analogue than to the natural pheromone (*E*11-14:Al), consonant with the importance of the hydrophobicity of the terminal methyl group.

We now describe the design and synthesis of fluorinated analogues of *Z*5-10:Ac in order to probe the importance of chain rigidity, polarity, and hydrophobicity in pheromone perception (Figure 1). Detailed electrophysiological and behavioral studies will be presented elsewhere.[16]

Results and Discussion

Starting from 5-hexyn-1-ol, the synthesis of the perfluorobutyl (Pfb) analogue 7,7,8,8,9,9,10,10,10-nonafluoro-*Z*5-10:Ac (**2**) was achieved in three steps with 60% overall yield (Figure 2). Thus, heating the alkynol and C_4F_9I at 80 °C for 20 h with a catalytic amount of azobis(isobutyronitrile) (AIBN) afforded 85% yield of the alkenyl iodides **7** as a 7:1 mixture.[17] As described previously,[11] the iodoalkene isomers were separated at this stage by flash column chromatography using SiO_2. Lithium–halogen exchange and low-temperature quenching of the pure *E* isomer at dilute concentration gave Pfb-*Z*5-10:OH (**8**) in 80% yield. It was important to keep the iodoalkenol concentration below 0.1 M to ensure clean and complete reaction because of the limited solubility of the dianion in ether. Acetylation of alkenol **8** gave excellent yield of the perfluorobutyl pheromone analogue **2**. It is worth reemphasizing that the separation of *E* and *Z* isomers by flash column chromatography was only possible on the perfluorobutyl alkenyl iodide **7**; all subsequent perfluorobutyl analogues were inseparable by silica gel chromatography.

The synthesis of 7,7,8,8-tetrafluoro-*Z*5-10:Ac (**3**) was achieved in seven steps with 12% overall yield (Figure 3). Using the literature procedure for addition of $CBrClF_2$ to an acetylenic anion,[18] the bromodifluoroacetylene **10** was prepared in 51% yield along with 25% of bromoacetylene **11**. These two compounds were difficult to separate by silica gel flash chromatography or by distillation. Lithium–halogen exchange reaction of the mixture in the presence of propionaldehyde[19] gave poor yield of the difluorohydrin **12**. In contrast, a quantitative yield of the difluorohydrin was obtained by stirring the mixture with zinc powder and propionaldehyde in THF at 0 °C.[20] The difluorohydrin **12** is easily separated from the unreacted bromoacetylene **11** by flash chromatography. Oxidation of **12** to the corresponding difluoromethylene ketone was achieved using CrO_3/pyridine in CH_2Cl_2. Pyridinium chlorochromate[21] and pyridinium dichromate[22] did not

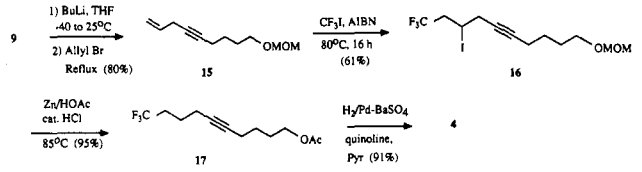

Figure 4. Synthesis of 10,10,10-trifluoro-*Z*5-10:Ac (**4**).

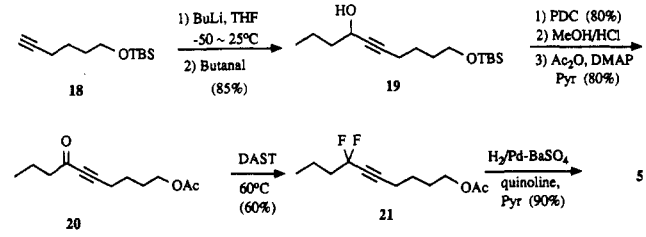

Figure 5. Synthesis of 7,7-difluoro-*Z*5-10:Ac (**5**).

effect this oxidation. Heating the difluoromethylene ketone with zinc powder in acetic acid allowed selective removal of the methoxymethyl (MOM) protecting group, providing the desired acetate **13** in 88% yield.

Attempted fluorination of the α,α-difluoroketone **13** with diethylaminosulfur trifluoride (DAST) at 80 °C for 72 h, with DAST and DMAP[23] or with DAST combined with anhydrous HF, all failed to provide tetrafluorinated products. The sluggish reactivity is most likely due to the highly stabilized difluoromethylene fluorohydrin formed as the first step of the carbonyl to difluoromethylene conversion. To circumvent this problem, we converted the ketone to a 1,3-dithiolane, followed by reaction with 1,3-dibromo-5,5-dimethylhydantoin (DBH) and pyridinium poly(HF) in CH_2Cl_2.[24] This also failed to provide the desired tetrafluoro compound; in this reaction sequence,[25] an allyl ether was employed as the protecting group during the dithiolane formation and attempted fluorination. A product involving participation of the allyl ether in the dithiolane fluorination was obtained.

Successful fluorination of the dilfuoromethylene ketone (as the acetate **13**) was eventually accomplished under forcing conditions by reaction with sulfur tetrafluoride.[26] This method is reported to require the presence of substantial amounts of HF to form the α,α-difluoro fluorohydrin, which then sluggishly undergoes C–O cleavage with displacement by fluoride even when SF_4 unmodified by deactivating amine ligands is employed. Thus, the reaction was carried out with an excess of SF_4 in a sealed, heavy-walled glass tube with the addition of water to generate HF in situ. After 18 h, the tetrafluoro acetate **14** was isolated in 60% yield. Semihydrogenation of **14** with quinoline-poisoned Pd–$BaSO_4$ provided the desired 7,7,8,8-tetrafluoro-*Z*5-10:Ac (**3**) in 91% yield.

Our initial attempt to synthesize the 10,10,10-trifluoro-*Z*5-10:Ac (**4**) via reductive coupling of trifluoropropylmagnesium iodide with a propargylic tosylate mediated by dilithium tetrachlorocuprate was unsuccessful.[25] Successful synthesis of the trifluoromethyl analogue **4** was achieved via a free radical addition of iodotrifluoromethane to an allyl alkyne (Figure 4). Thus, by heating enyne **15** with CF_3I and catalytic AIBN[17a] in a sealed, heavy-walled glass tube for 14 h, the adduct **16** was obtained in 61%

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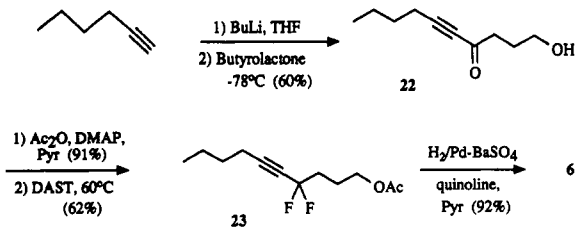

Figure 6. Synthesis of 4,4-difluoro-*Z*5-10:Ac (**6**).

yield. No products resulting from addition across the triple bond could be detected by GC–MS or by ^{1}H NMR. The iodotrifluoromethyl compound **16** was heated with zinc powder in acetic acid containing 2% HCl at 85 °C for 6 h. Under these conditions, the compound was deiodinated, deprotected, and also acetylated to give the desired 10,10,10-trifluoro-5-decynyl acetate (**17**) with over 90% yield. Semihydrogenation with quinoline-poisoned Pd-$BaSO_4$ in pyridine yielded the desired product 10,10,10-trifluoro-*Z*5-10:Ac (**4**).

The 7,7-difluoro-*Z*5-10:Ac (**5**) was synthesized in 18% overall yield (Figure 5). Freshly distilled butyraldehyde was added to the lithium acetylide of **18** to give the propargylic alcohol **19** in 85% yield. Oxidation of **19** followed by deprotection and acetylation provided the acetate **20** for fluorination. Heating **20** with DAST at 55 °C for 6 h afforded the propargylic difluoride **21** in 60% yield. Semihydrogenation with quinoline-poisoned Pd–$BaSO_4$ in pyridine afforded the 7,7-difluoro-*Z*5-10:Ac (**5**) in excellent yield.

The synthesis of 4,4-difluoro-*Z*5-10:Ac (**6**) was achieved in four steps in 35% overall yield from 1-hexyne (Figure 6). A solution of the lithium acetylide of 1-hexyne in THF was added to a solution of α-butyrolactone in THF at −78 °C. After 30 min, the reaction was quenched with NH_4Cl solution to give the hydroxy alkynone **22** in 60% yield. We noted that addition of the butyrolactone to the acetylide or quenching the reaction after warming up to room temperature gave the undesired tertiary alcohol arising from addition of a second molecule of acetylide to the initially produced ynone. Acetylation followed by fluorination with DAST provided the propargylic difluoride **23** in 55% yield (two steps). Semihydrogenation of the propargylic difluoride with quinoline-poisoned Pd–$BaSO_4$ in pyridine gave a quantatitive yield of 4,4-difluoro-*Z*5-10:Ac (**6**).

The strong inductive effect of fluorine can be best illustrated when it is close to a double bond. The induced partial negative charge at the atom which is closer to the fluorines was reflected on the NMR spectra. Thus, the olefinic proton on the carbon attached to the CF_2 group predictably exhibits an upfield chemical shift due to increased local shielding. Moreover, the difference of chemical shift between the two olefinic protons correlates roughly with the number of fluorines and with the distance to the fluorine substituent (Table I). In the instance of 10,10,10-trifluoro-*Z*5-10:Ac, even though the fluorines are five bonds away from the alkene, there was still a significant difference in the chemical shift between the vinylic protons. As one might expect, the carbon-13 chemical shifts also show similar characteristics.

The biological results[27] for selected compounds were quite intriguing. Single sensillum recordings showed that the difluoro, trifluoro, and tetrafluoro analogs **5**, **4**, and **3** are 100-fold less active than the parent *Z*5-10:Ac, while the nonafluoro analogue **2** was 10 000-fold less active. Unexpectedly, when **5**, **4**, or **3** was substituted for *Z*5-10:Ac in a three-component pheromone blend, the new blend was essentially equipotent to the natural pheromone blend in eliciting a behavioral response. Clearly, major alterations of the hydrophobicity and electronic character of pheromone chains can be tolerated by the pheromone perception system in this moth.

(27) Wu, W.; Bengtsson, M.; Hansson, B. S.; Liljefors, T.; Löfstedt, C.; Prestwich, G. D.; Sun, W.-C.; Svensson, M. Abstracts of the 8th Annual Meeting of the International Society of Chemical Ecology, Dijon, 1991.

Table I. Differences in Chemical Shift of Double-Bond Atoms

compd	Δppm ^{1}H	Δppm ^{13}C
Pfb-*Z*5-10:Ac	0.59	28.2
7,7,8,8-tetrafluoro-*Z*5-10:Ac	0.46	23.7
7,7-difluoro-*Z*5-10:Ac	0.32	12.9
4,4-difluoro-*Z*5-10:Ac	0.29	14.2
10,10,10-trifluoro-*Z*5-10:Ac[a]	0.06	2.4
*Z*5-10:Ac	0	0

[a] The assignment of chemical shift of this compound cannot be determined by the splitting pattern from the NMR spectra.

Experimental Section

General. Anhydrous THF and diethyl ether were distilled from sodium benzophenone ketyl prior to use. Thin-layer chromatography (TLC) was performed on silica gel plates (4 cm × 8 cm × 0.25 mm); the developed TLC plates were visualized by staining with either 3% vanillin (w/v) in 95% ethanol containing 0.33% of H_2SO_4 or 10% phosphomolybdic acid (w/v) in 95% ethanol. ^{1}H NMR (300-MHz) and ^{13}C NMR (75-MHz) spectra were obtained using 0.03% tetramethylsilane (TMS) as an internal standard in chloroform-d_3, and only key diagnostic data are presented herein. ^{19}F NMR (282 MHz) were obtained using $CFCl_3$ as an internal standard in acetone-d_6 or benzene-d_6, with chemical shifts (ϕ) in ppm upfield from $CFCl_3$. GC–mass spectra were obtained using a fused silica capillary column (HP-1) and a mass selective detector. Gas chromatography was carried out on a fused silica capillary column (DB-1 or DB-5, 0.263 mm i.d. × 30 m or HP-1, 0.32 mm × 25 m, 1-μm film thickness). Elemental analysis was performed by Oneida Research Services, Inc. All glassware, syringes, and needles were dried in an oven at 110 °C before use. The glassware was assembled hot and cooled under a flow of dry nitrogen. All of the reactions were carried out under a small positive pressure of dry nitrogen or argon, using a mercury bubbler as a pressure relief valve. The phrase "isolated as usual" means extraction with three portions of hexane or diethyl ether, washing with saturated brine, drying over $MgSO_4$, concentration in vacuo, and flash chromatography on 63–32-μm SiO_2 by elution with hexane–ethyl acetate mixtures.

5-Iodo-7,7,8,8,9,9,10,10,10-nonafluoro-5-decen-1-ol (7). 5-Hexyn-1-ol (980 mg, 10 mmol), *n*-perfluorobutyl iodide (5.2 g, 15 mmol), and AIBN (130 mg, 0.8 mmol) were placed in a heavy-walled glass tube (2.5-cm o.d., 1.8 cm i.d. × 20 cm, with a narrow neck 5 cm from bottom) equipped with a magnetic stir bar. The mixture was frozen (liq. N_2, 77 K), degassed, and thawed under nitrogen atmosphere to eliminate oxygen. This process was repeated, and the tube was sealed under vacuum while the contents were still frozen. The mixture was slowly warmed to room temperature and heated to 80 °C for 18 h. After being cooled with liquid N_2, the tube was broken open. The crude product was purified, and the *E* and *Z* isomers were separated by flash column chromatography (hexane–ethyl acetate (10:1)). Fractions with over 98% isomeric purity (GC) were combined; the remaining fractions were pooled, concentrated, and chromatographed again. After two chromatographic separations, two portions were obtained, geometrically pure *E* isomer of 5-iodo-Pfb-Δ5-10:OH (2.22 g, 50% yield) and a mixture of *E* and *Z* isomers of alkenyl iodide **7** (1.46 g, 33% yield). A small aliquot was analyzed by GC and indicated that before chromatography the *E*:*Z* ratio was 7:1: ^{1}H NMR δ 6.26 (t, J_{H6-F7} = 14.5 Hz, 1 H), 3.56 (t, J = 5.72 Hz, 2 H), 2.59 (t, J = 6.9 Hz, 2 H), 1.8–1.5 (m, 4 H); ^{19}F NMR ϕ 80.84 (t, F-10), 104.89 (m, 2 F), 123.65 (m, 2 F), 125.34 (m, 2 F).

(*Z*)-7,7,8,8,9,9,10,10,10-Nonafluoro-5-decen-1-ol (8). A solution of *n*-BuLi (1.6 M soln. in hexane, 3 mL) was added to a solution of **7** (444 mg, 1 mmol) in 10 mL of dry ether at −78 °C. The mixture was stirred for 30 min and quenched with precooled

(−78 °C) methanol (3 mL). After being warmed to 0 °C, the mixture was poured into 20 mL of NH_4Cl solution and the product was isolated as usual with ether to give 270 mg (85%) of Pfb-Z5-10:OH (8): ^1H NMR δ 6.12 (dtt, H-5, J_{H5-H6} = 12.2 Hz, J_{H5-H4} = 7.1 Hz, J_{H5-F7} = 2.4 Hz, 1 H), 5.53 (br q, H-6, J = 14.5 Hz, 1 H), 3.55 (t, H-1, J = 6.4 Hz, 2 H), 2.28 (br, H-4, 2 H), 1.6–1.5 (m, 4 H); ^{19}F NMR ϕ 80.79 (t, F-10), 104.33 (m, 2 F), 123.55 (m, 2 F), 125.63 (m, 2 F). Anal. Calcd for $C_{10}H_{11}F_9O$: C, 37.75; H, 3.48; F, 53.74. Found: C, 37.80; H, 3.41; F, 53.84.

(Z)-7,7,8,8,9,9,10,10,10-Nonafluoro-5-decenyl Acetate (2). A mixture of Pfb-Z5-10:OH (8) (27 mg, 0.1 mmol), acetic anhydride (36 mg, 0.3 mmol), and DMAP (5 mg) in 2 mL of pyridine was stirred at 25 °C for 1 h. The mixture was diluted with 30 mL of hexane–EtOAc (7:3) solution, washed (saturated $CuSO_4$), and the product isolated as usual to yield 32 mg (92%) of Pfb-Z5-10:Ac (2): ^1H NMR δ 6.12 (dtt, H-5, J_{H5-H6} = 12.2 Hz, J_{H5-H4} = 7.1 Hz, J_{H5-F7} = 2.4 Hz, 1 H), 5.53 (br q, H-6, J = 14.5 Hz, 1 H), 4.05 (t, H-1, J = 6.8 Hz, 2 H), 2.38 (br, H-4, 2 H), 2.02 (s, 3 H), 1.63 (quintet, 2 H), 1.52 (quintet, 2 H); ^{13}C NMR δ 171.02, 144.76, 116.58 (t, J = 23.4 Hz), 125–105 (many small multiplets), 64.00 (t, J = 8.5 Hz), 28.11 (t, J = 15.6 Hz), 25.50 (t, J = 18.6 Hz), 20.70 (t, J = 16.7 Hz); ^{19}F NMR showed the same resonances as for compound 8. Anal. Calcd for $C_{12}H_{13}F_9O_2$: C, 40.01; H, 3.64. Found: C, 40.09; H, 3.54.

5-Hexyn-1-yl Methoxymethyl Ether (9). NaH (4.2 g, 60% in mineral oil, 105 mmol) was washed with pentane (3 × 30 mL) and suspended in 200 mL of dry THF. A solution of 5-hexyn-1-ol (9.8 g, 100 mmol) in 30 mL of THF was added to the suspension at 0 °C and then brought to reflux for 1.5 h. After the solution was cooled to 25 °C, a solution of chloromethyl methyl ether (9.0 g, 112 mmol) in THF (20 mL) was added to the yellow suspension and the mixture was refluxed 3 h. After the mixture was cooled to 25 °C, water (250 mL) was added and the product was isolated (hexane) as usual to give 13.3 g (94%) of 9: ^1H NMR δ 4.60 (s, 2 H), 3.53 (t, H-1, J = 6.1 Hz, 2 H), 3.35 (s, 3 H), 2.22 (tt, H-4, J = 2.6 and 6.7 Hz, 2 H), 1.94 (t, H-6, J = 2.6 Hz, 1 H), 1.75–1.55 (m, H-3 and H-4, 4 H).

7-Bromo-7,7-difluoro-5-heptynyl Methoxymethyl Ether (10). *n*-BuLi (34 mL, 1.6 M in hexane) was added to a solution of 9 (7.10 g, 50 mmol) in THF (180 mL) at −40 °C. The mixture was allowed to warm to 25 °C and stirred for 1.5 h. $CBrClF_2$ was condensed into an addition funnel (16 mL) with a dry ice condenser and added to the above solution in one portion at −78 °C. The solution turned blood red upon addition of $CBrClF_2$. Stirring was continued for another 2 h at 78 °C. The reaction was quenched with NH_4Cl solution (100 mL) at −78 °C and extracted with hexane (3 × 50 mL). (Quenching after warming to 25 °C will give an undesired pigment which coelutes with the product.) The product was isolated as usual to give a mixture of bromodifluoromethyl acetylene 10 and bromoacetylene 11 (9.1 g); the yields estimated by GC (74:26 ratio) were 51% and 25%, respectively: ^1H NMR δ 4.62 (s, 2 H), 3.55 (t, H-1, J = 6.5 Hz, 2 H), 3.36 (s, 3 H), 2.41 (tt, H-4, J = 6.7 and 2.3 Hz, 2 H), 2.25 (t, H-4 or 13, J = 6.9 Hz), 1.6–1.3 (m br, H-2, H-3, 4 H); GC/MS (70 eV) m/z (rel intensity) 45 (100), 75 (35), 88 (23), 109 (27), 111 (13), 127 (15), 129 (28), 159 (9), 183 (15), 185 (15).

7,7-Difluoro-8-hydroxy-5-decyn-1-yl Methoxymethyl Ether (12). A solution of 10 (5.43 g, 74% mixture with 11, 14.7 mmol) in dry THF (10 mL) was added to a mixture of acid-washed zinc powder (2.6 g, 40 mmol) and freshly distilled propionaldehyde (1.26 g, 21 mmol) in dry THF (20 mL) at 0 °C. At least 2 hr prior to the addition, a 10-g portion of Zn powder had been acid-washed, rinsed with water, ethanol, and ether, and dried in vacuo. The mixture was stirred at 0 °C for 4 h, 5% HCl solution (30 mL) was added, and the mixture was stirred 5 min. Zinc was removed by filtration, and the product was isolated as usual from the filtrate to give 3.6 g (quantitative) of difluorohydrin 12. The bromoacetylene 11 was unreactive under this condition and was easily separated from 12 on SiO_2: ^1H NMR δ 4.62 (s, 2 H), 3.67 (m, H-8, 1 H), 3.55 (t, H-1, J = 6.5 Hz, 2 H), 3.36 (s, 3 H), 2.31 (m, H-4, 2 H), 1.8–1.5 (m br, 6 H), 1.06 (t, H-10, J = 7.4 Hz, 3 H).

7,7-Difluoro-8-oxo-5-decyn-1-yl Acetate (13). CrO_3 (6.0 g, 60 mmol) was added to a solution of pyridine (9.24 g, 120 mmol) in CH_2Cl_2 (50 mL) at 0 °C. The mixture was stirred at 0 °C for 1 h and then at 25 °C for 1 h. Difluorohydrin 12 (2.5 g, 10 mmol) in 5 mL of CH_2Cl_2 was added to the dark brown slurry in one portion. The mixture was stirred for another 10 h and was diluted with ether (200 mL). The supernatant was filtered through SiO_2 and concentrated in vacuo. The crude product was chromatographed with Et_3N, washed with silica gel, and eluted with hexane–EtOAc (90:10) containing 0.5% Et_3N: ^1H NMR δ 4.63 (s, 2 H), 3.53 (t, H-1, J = 5.8 Hz, 2 H), 3.35 (s, 3 H), 2.75 (q, H-9, J = 7.2 Hz, 2 H), 2.38 (m, H-4, 2 H), 1.69 (m, 4 H), 1.14 (t, H-10, J = 7.2 Hz, 3 H); GC/MS m/z 45 (81, $CH_2OCH_2^+$), 57 (100, $C_2H_5CO^+$), 88 (33), 115 (30) 187 (2, $M^+ - OCH_2OCH_3$), 203 (0.8, $M^+ - CH_2OCH_3$), 219 (0.8, M^+ − ethyl).

The difluoro ketone MOM ether obtained from the above reaction (120 mg, 0.5 mmol) and acid-washed zinc powder (65 mg, 1 mmol) in 2 mL of acetic acid was heated at 80 °C for 4 h. The mixture was diluted with water (20 mL) and extracted with hexane–EtOAc (70:30, 3 × 20 mL), and the product was isolated as usual (hexane–EtOAc (95:5) containing 1% Et_3N during SiO_2 chromatography) to yield 105 mg (88%) of the acetate 13: ^1H NMR δ 4.05 (t, H-acetate, J = 5.9 Hz, 2 H), 2.75 (q, H-9, J = 7.2 Hz, 2 H), 2.32 (m, H-4, 2 H), 1.69 (m, 4 H), 1.14 (t, H-10, J = 7.2 Hz, 3 H).

7,7,8,8-Tetrafluoro-5-decyn-1-yl Acetate (14). Sulfur tetrafluoride (SF_4, ca. 200 mg) was condensed (liquid N_2 bath) into a heavy-walled glass tube containing 13 (58 mg, 0.23 mmol) and water (25 mg) in 0.3 mL of CH_2Cl_2. The tube was sealed with a torch under vacuum line while the contents were still frozen in the liquid N_2 bath. After being stirred at 25 °C for 18 h, the black mixture was frozen in liquid N_2 again. The tube was cut at the top and opened with a hammer, and the mixture was diluted with ether; the ether extract was filtered (SiO_2), concentrated in vacuo, and chromatographed (hexane–EtOAc (95:5)) to yield 38 mg of 14 (60%): ^1H NMR δ 4.08 (t, H-1, J = 5.9 Hz, 2 H), 2.37 (m, H-4, 2 H), 2.06 (m, H-9, 2 H), 2.05 (s, H-acetate, 3 H), 1.8–1.6 (m, H-2 and H-4, 4 H), 1.10 (t, H-10, J = 7.5 Hz, 3 H); ^{13}C NMR δ 170.98 (C-ester), 118.54 (tt, J = 252 and 34 Hz), 109.04 (tt, J = 242 and 33 Hz), 91.46 (t, J = 6 Hz), 69.94 (t, J = 38 Hz), 63.56 (C-1), 27.63, 24.13, 23.94 (t, C-9, J = 23 Hz), 20.80, 18.14, 4.86 (t, C-10, J = 4 Hz); GC/MS m/z 43 (100, CH_3CO^+), 61 (58), 79 (98, $C_2H_5CF_2^+$), 88 (21), 101 (26), 129 (89, $C_2H_5C_2F_4^+$), 147 (14), 193 (11), 253 (2.2, $M^+ - CH_3$).

(Z)-7,7,8,8-Tetrafluoro-5-decen-1-yl Acetate (3). A mixture of Pd–$BaSO_4$ (15 mg) and quinoline (5 mg) in 2 mL of pyridine was stirred under a small positive pressure of H_2. A solution of 14 (33 mg) in 0.3 mL of pyridine was added to the above mixture in one portion after the catalyst turned black. Hydrogenation continued for another 45 min until there was no starting material left as determined by GC or by TLC. The product showed a higher spot on TLC plate with R_f (10% EtOAc–hexane) = 0.31 for starting material and 0.48 for the product. The catalyst was removed by filtration and washed with ether. The filtrate was diluted with 60 mL of hexane–EtOAc (70:30), washed with saturated $CuSO_4$ solution (20 mL × 3), dried ($MgSO_4$), concentrated in vacuo, and chromatographed (hexane–EtOAc (95:5)) to give 30 mg of 3 (91%): ^1H NMR δ 5.96 (dtt, H-5, J_{H5-H6} = 12 Hz, J_{H5-H4} = 7.8 Hz, J_{H5-F7} = 2.3 Hz, 1 H), 5.52 (m, H-6, 2 H), 4.05 (t, H-1, J = 6.5 Hz, 2 H), 2.32 (m br, H-4, 2 H), 2.03 (s, H-acetate, 3 H), 2.1–1.9 (m, H-9), 1.64 (m, 2 H), 1.48 (m, 2 H), 1.08 (t, H-10, J = 7.5 Hz, 3 H); ^{13}C NMR δ 171.08 (C-ester), 142.15 (t, J_{C5-F7} = 5 Hz), 118.46 (t, J = 24 Hz), 120–110 (m, C-7 and C-8), 64.14 (C-1), 28.08, 28.04, 25.58, 23.72 (t, C-9, J = 24 Hz), 20.87, 4.84 (t, C-10, J = 4 Hz); ^{19}F NMR ϕ 123.06 (br t, F-8, J = 19 Hz), 112.86 (br d, F-7, J = 15 Hz); GC/MS m/z 43 (100, CH_3CO^+), 81 (31), 103 (47), 111 (40), 131 (28), 190 (11), 210 (3, M^+ − HOAc), 228 (1.3). Anal. Calcd for $C_{12}H_{18}F_4O_2$: C, 53.33; H, 6.71; F, 28.12. Found: C, 53.15; H, 6.68; F, 28.11.

Non-5-yn-7-en-1-yl Methoxymethyl Ether (15). *n*-BuLi (3.8 mL, 1.6 M) was added to a solution of 9 (710 mg, 5 mmol) in 25 mL THF at −50 °C. The solution was warmed to 25 °C and stirred for 2 h. Freshly distilled allyl bromide (1.2 g, 10 mmol) was added to the acetylide solution at 25 °C. The solution was heated at reflux for 3 h and cooled to 25 °C, water was added, and the product was isolated as usual to give 730 mg (80%) of allyl acetylene 15: ^1H NMR δ 5.81 (ddt, H-8, $J_{H8-H9trans}$ = 16.9 Hz, $J_{H8-H9cis}$ = 10.0 Hz, J_{H8-H7} = 6.9 Hz, 1 H), 5.30 (dd, H-9 (trans), J = 15.3 and 1.7 Hz, 1 H), 5.08 (dd, H-9 (cis), J = 10.0 and 1.6 Hz, 1 H), 4.61 (s, 2 H), 3.54 (t, H-1, J = 6.2 Hz, 2 H), 3.35 (s, 3 H), 2.93 (br, H-7, 2 H), 2.24 (m, H-4, 2 H), 1.70 (quintet, J = 6.8

Hz, 2 H), 1.60 (quintet, J = 6.6 Hz, 2 H); GC/MS m/z 45 (100), 67 (42), 89 (53), 91 (60), 109 (20), 135 (30), 137 (20, $M^+ - CH_2OCH_3$), 141 (19, M^+ - allyl).

8-Iodo-10,10,10-trifluorodec-5-yn-1-yl Methoxymethyl Ether (16). Iodotrifluoromethane (1 g, 5.1 mmol) was condensed through a dry ice condenser into a heavy-walled glass tube containing **15** (364 mg, 2 mmol) and AIBN (26 mg, 0.8 mmol). The mixture was frozen (liquid N_2), degassed, and thawed under dry N_2. The process was repeated, and the tube was sealed with a torch (in vacuo). The tube was heated at 80 °C for 16 h, cooled with liquid N_2, and opened, and the crude product was chromatographed with hexane–EtOAc (95:5) to give 450 mg (61%) of **16**: ^{1}H NMR δ 4.62 (s, 2 H), 4.23 (quintet, H-8, J = 6.3 Hz, 1 H), 3.55 (t, H-1, J = 6.4 Hz, 2 H), 3.36 (s, 3 H), 3.1–2.9 (m, H-9, 2 H), 2.85 (m, H-7, 2 H), 2.23 (m, H-4, 2 H), 1.72 (m, 2 H), 1.62 (m, 2 H); GC/MS m/z 45 (100), 79 (16), 91 (14), 101 (12), 127 (10), 142 (8), 149 (7), 175 (6), 191 (20), 219 (18), 251 (0.8, M^+ - 127), 333 (1, $M^+ - CH_2OCH_3$), 347 (2, $M^+ - OCH_3$).

10,10,10-Trifluorodec-5-yn-1-yl Acetate (17). A mixture of **16** (110 mg, 0.29 mmol) and acid-washed zinc powder (150 mg) in 1.7 mL of HOAc containing 2% of HCl was heated at 85 °C for 4 h. The mixture was diluted with 20 mL of water and extracted with hexane, and the product isolated as usual to give 73 mg (95%) of 10,10,10-trifluoro-Z5-10:Ac **17**: ^{1}H NMR δ 4.04 (t, H-1, J = 6.4 Hz, 2 H), 2.20 (m, H-4 H-6, 4 H), 2.01 (s, H-acetate, 3 H), 1.71 (m, H-9, 2 H), 1.62 (m, 2 H), 1.5 (m, 2 H). Anal. Calcd for $C_{12}H_{17}F_3O_2$: C, 57.59; H, 6.85. Found: C, 57.61; H, 6.72.

(Z)-10,10,10-Trifluoro-5-decen-1-yl Acetate (4). Using a similar procedure for semihydrogenation of **3**, compound **4** was obtained in 91% yield from **17**: ^{1}H NMR δ 5.38 (m, H-5 H-6, 2 H), 4.06 (t, H-1, J = 6.7 Hz, 2 H), 2.06 (m, H-4 H-7, 4 H), 2.05 (s, H-acetate 3 H), 1.63 (m, 4 H), 1.42 (m, 2 H), 1.28 (br, 2 H); ^{13}C NMR δ 171.05 (C-ester), 130.78, 128.38, 126.88 (q, C-10, J = 276 Hz), 64.29 (C-1), 33.17 (q, C-9, J = 28 Hz), 28.20, 26.75, 26.04, 28.88, 21.86, 20.85; ^{19}F NMR ϕ 71.71 (t, J = 11.0 Hz). Anal. Calcd for $C_{12}H_{19}F_3O_2$: C, 57.71; H, 7.59; F, 22.59. Found: C, 57.28; H, 7.57; F, 22.82.

7-Hydroxy-5-decyn-1-yl *tert*-Butyldimethylsilyl Ether (19). n-BuLi (4.0 mL, 1.6 M), was added to a solution of **18** (1.35 g, 6.4 mmol) in 12 mL of ether at −50 °C. The solution was warmed to 25 °C stirred for 1.5 h. Freshly distilled butyraldehyde (740 mg, 10 mmol) was added to the above solution at −78 °C; the yellow color of the acetylide disappeared upon addition of aldehyde. The cooling bath was removed, water was added, and the product was isolated as usual to give 1.55 g (85%) of the propargylic alcohol **19**: ^{1}H NMR δ 4.38 (t, H-7, J = 6.3 Hz, 1 H), 3.62 (t, J = 6.1 Hz, 2 H), 2.23 (td, H-4, J = 7.2 and 2.0 Hz, 2 H), 1.6 (m, 6 H), 0.92 (t, H-10, J = 7.2 Hz, 3 H), 0.90 (s, 9 H), 0.05 (s, 6 H).

7-Oxo-5-decyn-1-yl Acetate (20). Oxidation[22] with PDC gave the corresponding silyl ether in 80% yield after chromatography: ^{1}H NMR δ 3.58 (t, H-1, J = 6.1 Hz, 2 H), 2.48 (t, J = 7.2 Hz, 2 H), 2.39 (t, J = 6.9 Hz, 2 H), 1.7 (m, 6 H), 0.93 (t, H-10, J = 7.4 Hz, 3 H), 0.90 (s, 9 H), 0.05 (s, 6 H).

The crude silyl ether ketone obtained from the above reaction was stirred with 2% methanolic HCl for 3 h at 25 °C. The solution was diluted with water and the alcohol product was isolated as usual (90%): ^{1}H NMR δ 3.68 (t, J = 6.1 Hz, 2 H), 2.51 (t, J = 7.2 Hz, 2 H), 2.42 (t, J = 6.9 Hz, 2 H), 1.7 (m, 6 H), 0.93 (t, H-10, J = 7.4 Hz, 3 H).

Acetylation was accomplished using a similar procedure for preparation of compound **2** to give the acetate **20**: ^{1}H NMR δ 4.07 (t, J = 6.2 Hz, 2 H), 2.49 (t, J = 7.3 Hz, 2 H), 2.40 (t, J = 6.9 Hz, 2 H), 2.04 (s, 3 H), 1.8–1.6 (m, 6 H), 0.93 (t, H-10, J = 7.4 Hz, 3 H).

7,7-Difluoro-5-decyn-1-yl Acetate (21). A mixture of DAST (161 mg, 1 mmol) and **20** (39 mg, 0.2 mmol) was heated at 55 °C for 6 h. The resulting dark brown mixture was poured into ice–water (10 mL) and extracted with hexane (3 × 10 mL), and the product was isolated as usual to give 26 mg (60%) of **21**: ^{1}H NMR δ 4.09 (t, J = 6.2 Hz, 2 H), 2.32 (tt, H-4, J = 6.7 and 1.9 Hz, 2 H), 2.05 (s, 3 H), 1.95 (m, H-8, 2 H), 1.73 (m, 2 H), 1.61 (m, 4 H), 0.98 (t, H-10, J = 7.4 Hz, 3 H); ^{19}F NMR ϕ 85.67 (tt, J_{F7-H8} = 14.6 Hz, J_{F7-H4} = 4.9 Hz). Anal. Calcd for $C_{12}H_{18}F_2O_2$: C, 62.05; H, 7.81. Found: C, 62.13; H, 7.88.

(Z)-7,7-Difluoro-5-decen-1-yl Acetate (5). Using a similar procedure for semihydrogenation of **3**, compound **5** was obtained in 90% yield from **21**: ^{1}H NMR δ 5.81 (dtt, H-5, J_{H5-H6} = 11.5 Hz, J_{H5-H4} = 7.7 Hz, J_{H5-F7} = 1.8 Hz, 1 H), 5.49 (dtt, H-6, J_{H6-F7} = 14.2 Hz, J_{H6-H5} = 11.8 Hz, J_{H6-H4} = 1.5 Hz, 1 H), 4.06 (t, H-1, J = 6.3 Hz, 2 H), 2.20 (br, H-4, 2 H), 2.04 (s, 3 H), 1.90 (m, H-8, 2 H), 1.65 (m, H-9, 2 H), 1.55 (m, H-2 H-3, 4 H), 0.95 (t, H-10, J = 7.2 Hz, 3 H); ^{13}C NMR δ 171.02, 137.88 (t, C-5, J_{C5-F7} = 6 Hz), 124.98 (t, C-6, J_{C6-F7} = 28 Hz), 121.16 (t, C-7, J_{C7-F7} = 237 Hz), 63.50 (C-1), 34.54 (t, C-8, J_{C8-F7} = 27 Hz), 34.78, 31.54, 22.26, 21.90, 20.68 (C-acetate), 15.33 (C-10); ^{19}F NMR ϕ 95.84 (multiplet). Anal. Calcd for $C_{12}H_{20}F_2O_2$: C, 61.52; H, 8.60; F, 16.22. Found: C, 61.75; H, 8.67; F, 15.75.

4-Oxo-5-decyn-1-ol (22). A solution of n-BuLi (13 mL, 1.6 M) and 1-hexyne (1.64 g, 20 mmol) in 50 mL of dry THF was stirred at 25 °C for 2 h. The resulting yellow solution was added to a solution of butyrolactone (2.6 g, 30 mmol) in 20 mL of dry THF at −78 °C through a syringe. The solution was stirred at −78 °C for 20 min, quenched with 10 mL of methanol, and warmed to 0 °C. Water was added, and the product was isolated with ether to give 2.01 g (60%) of **22**: ^{1}H NMR δ 3.61 (t, H-1, J = 6.2 Hz, 2 H), 2.63 (t, H-7, J = 7.1 Hz, 2 H), 2.33 (t, H-3, J = 7.1 Hz, 2 H), 1.86 (quintet, H-2, J = 6.7 Hz, 2 H), 1.53 (quintet, H-8, J = 7.2 Hz, 2 H), 1.40 (septet, H-9, J = 7.2 Hz, 2 H), 0.88 (t, H-10, J = 7.2 Hz, 3 H).

4,4-Difluoro-5-decyn-1-yl Acetate (23). Acetylation of alcohol **22** according to the procedure described for compound **2** gave the desired keto acetate: ^{1}H NMR δ 4.08 (t, H-1, J = 6.4, 2 H), 2.62 (t, H-7, J = 7.3 Hz, 2 H), 2.36 (t, H-3, J = 7.0 Hz, 2 H), 1.98 (quintet, H-2, J = 6.8 Hz, 2 H), 1.55 (quintet, H-8, J = 7.2 Hz, 2 H), 1.43 (septet, H-9, J = 7.4 Hz, 2 H). Next, fluorination according to the procedure described for compound **21** gave the desired acetate **23**: ^{1}H NMR δ 4.10 (t, H-1, J = 6.8 Hz, 2 H), 2.28 (m, H-7, 2 H), 2.05 (s, 3 H), 2.1 (m, 2 H), 1.89 (m, 2 H), 1.6–1.4 (m, 4 H), 0.95 (t, H-10, J = 7.3 Hz, 3 H). Anal. Calcd for $C_{12}H_{18}F_2O_2$: C, 62.05; H, 7.81. Found: C, 62.02; H, 7.74.

4,4-Difluoro-5-decenyl Acetate (6). Using a similar procedure for semihydrogenation of **3**, compound **6** was obtained in 92% yield from **23**: ^{1}H NMR δ 5.75 (dtt, H-6, J_{H6-H5} = 11.8 Hz, J_{H6-H7} = 7.8 Hz, J_{H6-F4} = 1.8 Hz, 1 H), 5.46 (dtt, H-5, J_{H5-F4} = 14.2 Hz, J_{H5-H6} = 12.0 Hz, J_{H5-H7} = 1.4 Hz, 1 H), 4.09 (t, H-1, J = 6.3 Hz, 2 H), 2.23 (br, H-7, 2 H), 2.05 (s, 3 H), 1.95 (m, H-3, 2 H), 1.84 (m, H-2, 2 H), 1.35 (m, H-8 H-9, 4 H), 0.90 (t, H-10, J = 7.2 Hz, 3 H); ^{13}C NMR δ 170.92, 138.54 (t, C-6, J_{C6-F4} = 6 Hz), 124.28 (t, C-5, J_{C5-F4} = 27 Hz), 122.22 (t, C-4, J_{C4-F4} = 240 Hz), 63.64 (C-1), 35.14 (t, C-3, J_{C3-F4} = 27 Hz), 34.78 (C-7), 31.54 (C-8), 22.26 (C-9), 21.90 (C-2), 20.83 (C-acetate), 13.83 (C-10); ^{19}F NMR ϕ 96.32 (multiplet). Anal. Calcd for $C_{12}H_{20}F_2O_2$: C, 61.52; H, 8.60. Found: C, 61.30; H, 8.70.

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Supplementary Material Available: ^{1}H and ^{13}C NMR spectra for final compounds 1–6 and also intermediate compounds **7**, **10**, **15–17**, and **19–23** (21 pages). Ordering information is given on any current masthead page.