Monofluoro Analogs of Eugenol Methyl Ether as Novel Attractants for the Oriental Fruit Fly

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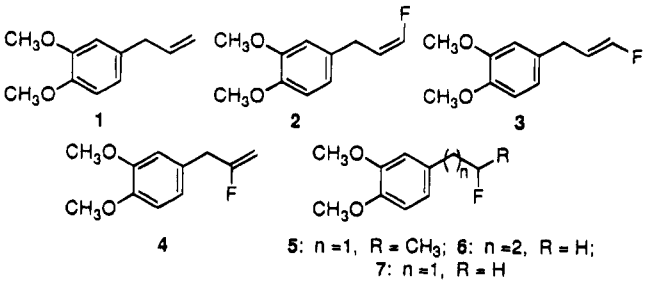
Monofluoro analogs of eugenol methyl ether as potential attractants for the Oriental fruit fly (*Bactrocera dorsalis*, Hendel) were synthesized using selective fluorination reactions: electrophilic hydro- and iodofluorination, fluorodehydroxylation with (diethylamido)sulfur trifluoride (DAST), and Wittig fluoroolefination through the stabilized ylides. Unusual reduction of the double bond was detected in a reaction of eugenol methyl ether with pyridinium poly(hydrogen fluoride). Bis-[(3,4-dimethoxyphenyl)alkyl] carbonates were identified as the novel nucleophilic substitution products of the intermediate generated from the reaction of 3,4-dimethoxybenzenealkanols with DAST. Reductive desulfonylation of fluorovinyl sulfone **24**-*(Z)* with sodium amalgam afforded 1,2-dimethoxy-4-(3-fluoro-2-propenyl)benzene (*E*/*Z* = 85:15) which was highly attractive to the Oriental fruit fly.

Eugenol methyl ether (**1**, Scheme 1) is an extremely potent and specific attractant for the Oriental fruit fly, a major pest of a wide variety of plant species.[1] This natural phenylpropanoid is successfully used to detect, monitor, and, in conjunction with a toxicant, eradicate the fly.[2] Reports indicating that **1** causes hepatic tumors in mice,[3a] induces intrachromosomal recombination in a yeast assay,[3b] and elicits a positive response in a bacterial DNA repair test[3c] could threaten its use in pest management programs. Metabolic activation of eugenol methyl ether is regarded to be a necessary prerequisite for potential toxicity and carcinogenicity.[3a,4] It has been suggested that enzymatic oxidation of the methylene group and/or epoxidation of the double bond might form ultimate carcinogens.[3a,4]

A number of reports describe introduction of a fluorine atom (as an isosteric replacement for hydrogen) into the vicinity of double bond to enhance metabolic or chemical stability[5] with minimal influence on the biological profile. Camps et al. mentioned modest deactivation of a fluoroolefinic moiety toward peracid epoxidation.[5a] Allylic difluorination was reportedly very efficient in blocking microsomal oxidation of some pyrethroids.[5b] The profound effect of fluorine incorporation on the reactivity of geminal and vicinal H-atoms could be exemplified by blocking enzymatic hydroxylation of vitamin D_3[5c] and the sex pheromone of the housefly.[5d] Hence, introduction of fluorine in the side chain of **1** might hinder metabolic oxidation. Alternatively, terminal fluoroolefins (e.g. **2** and **3**) may be efficient inhibitors[6] of the enzymes that catalyze an oxidation step of the allylic CH_2 of eugenol methyl ether.

Scheme 1



During the past decade, fluorinated pheromones,[7] pyrethroids,[5b] juvenile hormones,[5a,7] and green-leaf volatiles[8] have been synthesized and studied as new selective biochemical approaches toward insect control. In this study, we initiated research on fluorinated phenylpropanoids, the plant kairomones of a variety of insects.[1] Six monofluoro analogs of **1** (Scheme 1) were selected for synthesis and biological evaluation. In addition to unsaturated analogs **2**, **3**, and **4**, nonolefinic derivatives **5** and **6** were also studied. The fluoroethyl analog **7**, with a carbon shorter side chain, was of particular interest

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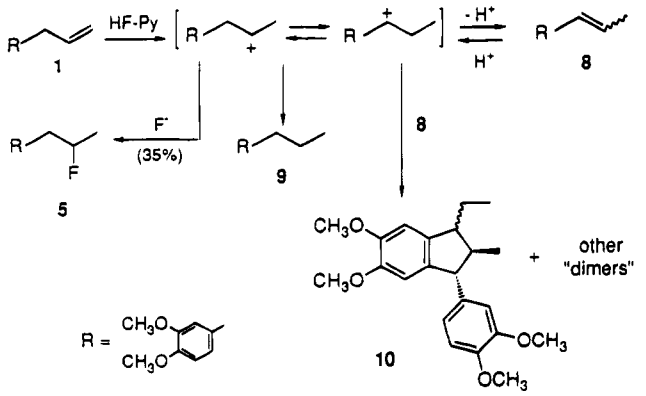
Scheme 2



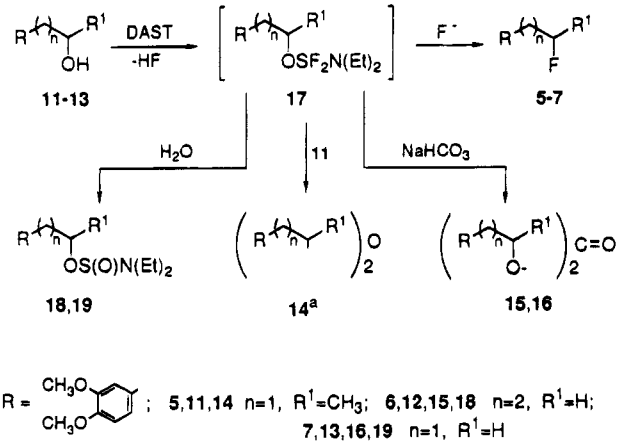
since its nonfluorinated counterpart was appreciably attractive to the Oriental fruit fly.[1] Analogs bearing fluorine at the α-position to the aromatic ring were omitted because of expected chemical or biochemical instability.

Results and Discussion

Hydrofluorination of eugenol methyl ether was viewed[9] as the most convenient approach to fluoride **5**. However, reaction of **1** with pyridinium poly(hydrogen fluoride) (HF·Py) in THF provided only 35% yield of desired product, the main reaction pathway being dimerization (Scheme 2). Flash chromatography of the reaction mixture afforded a fraction consisting of five compounds with M^+ 356 (GC-MS). Two of them were identified as *cis,trans*- and *trans,trans*-indans **10** (15% and 5%, respectively), prepared unambiguosly by HF·Py-catalyzed dimerization of *iso*-eugenol methyl ether (**8**, E/Z = 95:5). The latter reaction, initiated for the synthesis of a benzylic-type fluoro analog, proceeded without noticable sign of fluorination and afforded a 78% yield of 1,2-*trans*-2,3-*cis*- and 1,2-*trans*-2,3-*trans*-indans **10** in a ratio of 93:7. High yield and stereoselectivity of indan formation from **8** are consistant with other examples of acid-catalyzed dimerization of arylpropenes.[10,11] Nonetheless, conversion of **8** to indan **10** with HF·Py proceeded smoothly at 0 °C, while trifluoroacetic[10] and 40% sulfuric acid[11] reportedly catalyzed dimerization at room temperature and under reflux conditions, respectively.

Generation of a benzylic cation and deprotonation of the latter to **8** appear necessary for indan formation, and the interconversion of homobenzylic and benzylic cations under similar conditions has been described.[12] Other dimers, presumably arising from trapping of both cations by **1** through Friedel–Crafts alkylation, were not identified. Surprisingly, fluorobenzene **5** was contaminated with 7–10% of **9**, which was removed by flash chromatography. Reduction of double bond does not seem to occur with HF·Py but was recently discovered by Olah et al.[13] in a fluorination study of 1-phenyl-cycloalkenes with poly-4-vinylpyridinium poly(hydrogen fluoride), a solid hydrogen fluoride equivalent. However, their interpretation of this phenomenon was hydride donation from a polymer backbone to a cationic intermediate.

Scheme 3



[a] isolated as a 1:1 mixture of diastereomers

Fluorodehydroxylation with DAST, explored for the synthesis of saturated fluoro analogs of **1**, has already been reported with alcohols **12**[14] and **13**.[15] However, we obtained only a 49% yield of fluoride **6**, instead of the reported 91%,[14] when the reaction of **12** with DAST was conducted at 0–5 °C for 3 h with subsequent treatment with Na_2CO_3. Two additional products, identified as diethylamino sulfinate **18** and carbonate **15**, as well as starting alcohol, were isolated from the crude mixture (Scheme 3). In contrast, reaction of **13** with DAST (5 h, room temperature) afforded a 73% yield of **7** (reported[15] 70%) with no significant byproducts. Thus, we became interested in optimizing the conditions for synthesis of fluorides **5–7** and studying the reaction course of alcohols **11–13** with DAST. We found that slow addition of DAST to CH_2Cl_2 solutions of alcohols **12** and **13** at −45 to −50 °C, followed by warming to −30 °C and workup with sodium carbonate or bicarbonate, largely afforded sulfinates **18**, **19** and carbonates **15**, **16** (experiments d and f). In the case of secondary alcohol **11**, the corresponding sulfinate and carbonate were not found after a 4 h exposure at room temperature, but another byproduct, identified as ether **14**, was isolated in 31% yield (experiment b). Additional stirring of the reaction mixture at ambient temperature (experiments a, c, and e) led to the formation of fluorides **5–7** in high yields, with essentially no byproducts being isolated. Diethylamino sulfinates **18** and **19** appear to be the hydrolysis products of (diethylamino)sulfonium difluoride **17**, the well-accepted intermediate in the fluorination of alcohols with DAST.[16] However, the carbonates arising, presumably, from the nucleophilic substitution of the intermediate **17** have not been found in other cases of the fluorination using workup with $NaHCO_3$ or Na_2CO_3.[14,16] The ether **14**, apparently formed by reaction of the intermediate **17** with unreacted alcohol **11**,[17] could eventually be cleaved with HF, generated in the first step of the reaction, to form fluoride **5**. It can be concluded that the somewhat

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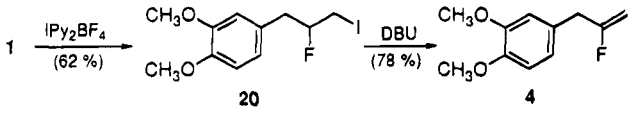
(17) An example of etherification in the reaction of DAST with diarylcarbinols was described: Johnson, A. L. *J. Org. Chem.* **1982**, *47*, 5220.

Scheme 4



forcing fluorination conditions required for the aromatic alcohols **11**–**13** with DAST (compared to the aliphatic alcohols[16]) are due to a sluggish nucleophilic displacement of intermediate **17** with fluoride ion. Possibly the electron-rich dimethoxyphenyl ring, capable of efficient π-complexation with HF, discourages protonation of the leaving group.

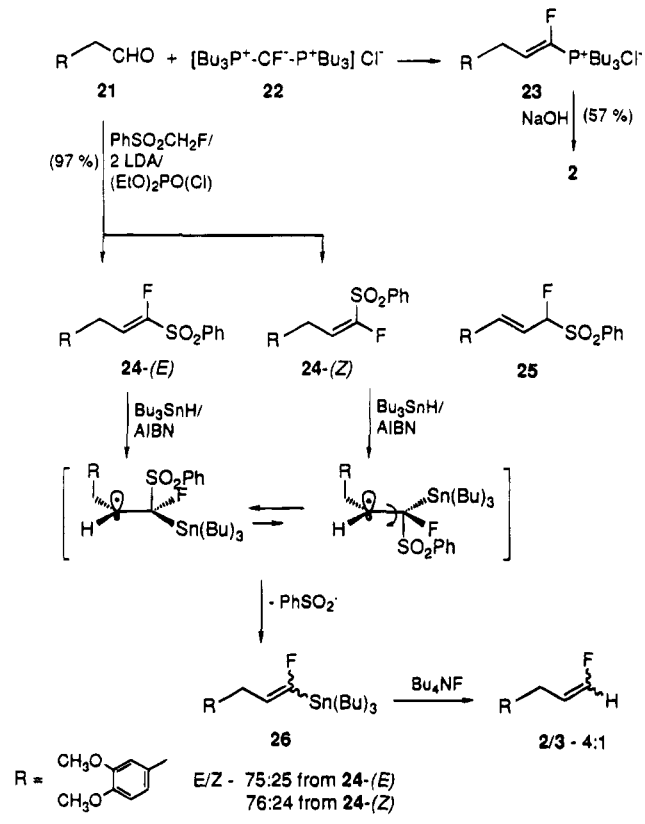
β-Fluoro analog **4** was conveniently prepared using sequential iodofluorination and dehydroiodination reactions.[18] Iodofluorination of **1** with bis(pyridine)iodonium(I) tetrafluoroborate[18] at −70 °C proceeded without significant side reactions[19] and provided fluoro iodide **20** in 62% yield. Dehydroiodination of **20** with DBU afforded a high yield of fluoroalkene **4** (Scheme 4).

One of the the major challenges of terminal fluoroolefins is stereospecific synthesis of both geometric isomers,[6a] separation of which is often difficult. Reaction of *N*-fluoro-*N*-alkyl sulfonamides with alkenyllithium reagents was reported to proceed with retention of configuration and provided fluoroalkenes contaminated with 5–15% of nonfluorinated olefin.[20] Wittig reaction through stabilized ylides was explored to achieve efficient stereocontrol[21,22] or to obtain readily separable sulfonyl derivatives of *(E)*- and *(Z)*-fluoroolefins that could be stereospecifically converted to final products.[6d,23,24] We examined aldehyde **21** in a Wittig reaction with phosphoranium salt **22**, developed by Cox et al.,[21,22] and found excellent stereocontrol, similar to that reported for aliphatic aldehydes[21] (Scheme 5). Stereospecific alkaline hydrolysis of the intermediate salt **23** afforded fluoroolefin **2** (*Z*/*E* = 97:3) in 57% overall yield.

Wittig–Horner reaction of aldehyde **21** with an ylide generated from fluoromethyl phenyl sulfone[23] provided almost quantitative olefination, giving a 3:2 mixture of *(E)*- and *(Z)*-fluorovinyl sulfones **24** (Scheme 5). Care had to be taken to avoid base-catalyzed isomerization of **24** to allylic sulfone **25**,[25] since a slight excess of LDA and/or warming the reaction mixture to ambient temperature promoted this side reaction. Although the Wittig–Horner olefination lacked stereoselectivity,[26] *(E)*- and *(Z)*-isomers of **24** could be separated with 92% and 93% geometrical purity by fractional crystallization from ethanol.

Conversion of fluorovinyl sulfones, obtained from ketones, to the corresponding stannanes is known to proceed with complete retention of configuration.[24,27] The only aldehyde investigated gave nonstereoselective

Scheme 5



results.[6d] However, data were insufficient to assess the degree of stereoselectivity for both geometric isomers. In our studies, stannylation of **24**-*(E)* and **24**-*(Z)* with tributyltin hydride provided almost identical mixtures of products (Scheme 5). If sulfone **24**-*(E)* reacted with partial loss of geometry (92% to 75%), the **24**-*(Z)* isomer underwent inversion of configuration (93% *Z* to 76% *E*). Assignment of geometric (fluorovinyl)stannanes **26** was made using $^3J_{CH=CF}$ vicinal coupling constants.[28] The stereochemical results of stannylation can be rationalized if one considers either addition–elimination[29] or single electron transfer[30] mechanisms of the homolytic substitution. However, the first interpretation, presuming equilibrium of intermediate radicals favoring sterically less hindered one, seems to be more appropriate (Scheme 5). As stannane **26** was appropriate only for synthesizing a mixture of fluoroolefins with **2** predominating (Scheme 5), we sought a method to prepare the *(E)*-analog **3** directly from sulfone **24**-*(Z)*.

Amalgamated aluminum, the only reagent used to reduce 1-fluoro-1-alkenyl sulfones,[23,31] failed to efficiently cleave sulfone **24**.[32] Other reducing agents,[33,34] known to stereoselectively remove a phenylsulfonyl group from

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(20) Lee, S. H.; Schwartz, J. *J. Am. Chem. Soc.* **1986**, *108*, 2445.
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(25) *(E)*-configuration of **25** was assigned on the basis of $^3J_{CH=CH}$ = 16.2 Hz.
(26) Poor stereoselectivity was observed with other aldehydes, e.g. see ref 23.
(27) McCarthy, J. R.; Matthews, D. P.; Paolini, J. P. *Org. Synth.* **1993**, *72*, 216.
(28) The magnitudes of these couplings: 53.0 and 36.0 Hz for **26**-*(E)* and **26**-*(Z)*, respectively, are consistent with data reported in ref 6d (supplementary material).
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(32) Reaction was very sluggish and also gave isomerization product **25**.
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Table 1. Reduction of Fluorovinyl Sulfones 24 with Sodium Amalgam

entry	sulfone 24 Z/E	reaction temp (°C), time	products,[a] % 3	2	1	8
1.	2:3	25, 20 min	44	29	17	8
2.	2:3	−20, 2 h	50	32	16	1
3.	7:92	−20, 2 h	42	37	18	1
4.	93:7	−20, 2 h	72	13	14	
5.	7:92	−45-(−50), 6 h	40	42	16	1
6.	93:7	−45-(−50), 10 h	73	13	13	

[a] Calculated from GC data.

vinyl sulfones, caused side reactions.[35] Sodium amalgam (2%) in Na_2HPO_4-buffered methanol[36] rapidly reduced fluoro sulfone **24** over a wide temperature range (Table 1). At 25 °C (entry 1), besides reductive desulfonylation products **2** and **3**, **1** and **8** were also detected by GC, indicating nonchemoselectivity of reduction. Formation of **8** implies that some isomerization of double bond also occurred. When the reaction was carried out at −20 °C (entry 2), no visible prototropic rearrangement took place, although reduction of both functionalities (16% **1**) was still observed. Since **1** could be completely removed from the mixture by chromatography on $AgNO_3$−SiO_2, we examined sulfones **24**-(E) and **24**-(Z) in this reaction. Reduction of **24**-(E) lacked stereoselectivity, affording about a 1:1 mixture of fluoroolefins **2** and **3** (entry 3). Appreciably better stereochemical results were obtained with **24**-(Z), when geometric purity dropped from 93% to only 85% (entry 4). The yield of fluoroolefin **3** (E/Z = 85:15) after argentation chromatography was 70%. A decrease of reaction temperature did not improve either stereochemistry or chemoselectivity (entries 5 and 6).

Fluoroolefin **3** demonstrated nearly the same beneficial attractiveness as eugenol methyl ether in several field tests against the Oriental fruit fly.[37] Even a 1.6:1 mixture of geometric isomers **3** and **2**, readily available in 67% total yield from aldehyde **21**, was appreciably active. Pure **2** showed substantially lower activity. Our further study will be focused on synthesis and evaluation of the pure *(E)*-analog **3**. Complete field bioassay with all monofluoro analogs of eugenol methyl ether will be published elsewhere. Toxicity studies of selected compounds are in progress.

Experimental Section

All reactions were performed under an atmosphere of dry N_2. THF was distilled from sodium benzophenone ketyl. Anhydrous CH_2Cl_2 was prepared by distillation from CaH_2. All organic reagents were purchased from Aldrich Chemical Co. unless otherwise noted. Eugenol methyl ether and *iso*-eugenol methyl ether were distilled prior to use. Aldehyde **21** was synthesized according to a known procedure.[38] Alcohol **11** was prepared in 91% yield by reaction of aldehyde **21** with 1.1 equiv CH_3MgCl in THF at −70 °C. ^1H NMR data of **11** are consistent with those reported in the literature.[39] Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN.

1,2-Dimethoxy-4-(2-fluoropropyl)benzene (5). Eugenol methyl ether (1.78 g, 10 mmol) was added to a solution of HF·Py (70:30, 10 mL, 35 mmol) in THF (2.5 mL) at 0 °C. The reaction mixture was stirred at 0 °C 1 h and then at 25 °C 18 h. The resulting solution was poured into ice−water and extracted with chloroform. The chloroform extract was washed with $NaHCO_3$ solution and water and dried (Na_2SO_4). Evaporation of the solvent and vacuum distillation (73−75 °C/0.25 mm) afforded 810 mg mixture of **5** and **9** (identified by GC-MS) with the ratio 93:7. Flash chromatography of that mixture with hexane (h)/ethyl acetate (ea) 5:1 provided 700 mg (35%) of fluoride **5**. ^1H NMR (300 MHz, $CDCl_3$/TMS): 1.35 (dd, 3H, $^3J_{HH}$ = 6.0, $^3J_{HF}$ = 23.7 Hz), 2.86 (m, 2H), 3.86 and 3.88 (s, 3H), 4.84 (dtq, 1H, $^2J_{HF}$ = 48.3, $^3J_{HH}$ = 6.0 Hz), 6.73−6.84 (m, 3H). ^{19}F NMR (283 MHz, $CDCl_3/CCl_3F$): 171.3 (dtq). MS (EI): M^+ 198 (28), 151 (100). Anal. Found: C, 66.45; H, 7.50. $C_{11}H_{15}FO_2$ requires: C, 66.63; H,7.64. Column chromatography (h/ea, 25:1 to 1:1) of the pot residue after distillation afforded a fraction with R_f 0.38 (h/ea, 7:3), consisting of five compounds (GC-MS) with M^+ 356. Two were identified as indans **10**.

1-(3,4-Dimethoxyphenyl)-2-methyl-3-ethyl-5,6-dimethoxyindan (10). *iso*-Eugenol methyl ether (**8**) (0.9 g, 5 mmol, *E*/*Z*, 95:5) was added to HF·Py (5 mL, 17 mmol) at 0 °C. The solution was kept at 0 °C for 18 h. Usual workup described above followed by flash chromatography (h/ea, 2:1) afforded 700 mg (78%) **10** as a 93:7 mixture of 1,2-*trans*-2,3-*cis* and 1,2-*trans*-2,3-*trans* isomers, respectively. Mp: 96−97 °C. ^1H NMR: 1.05 (d, 3H, J = 6.6 Hz, 2-CH_3, *trans,cis*), 1.17 (d, J = 6.6 Hz, 2−CH_3, *trans,trans*).[11] Other signals are consistent with those reported for the *trans,cis*-isomer.[40] MS (EI): *trans,cis*-**10**, M^+ 356 (91), 327 (100), 218 (13), 189 (16); *trans,trans*-**10**, M^+ 356 (100), 327 (82).

Reaction of Alcohols 11−13 with DAST. (a) DAST (5.35 mL, 40.5 mmol) was added slowly to a solution of **11** (5.3 g, 27 mmol) in CH_2Cl_2 (30 mL) at −60 °C. The mixture was allowed to warm to 20 °C and stirred for 20 h. The resulting solution was poured into ice−water and extracted with $CHCl_3$. The extract was washed with water, $NaHCO_3$ solution, and water and dried. Concentration and flash chromatography (h/ea, 7:5 then 1:2) afforded 3.74 g (70%) of fluoride **5** (98% purity by GC) and 510 mg (10%) of starting alcohol **11**.

(b) Analogously, reaction of alcohol **11** (480 mg, 2.45 mmol) with DAST (0.343 mL, 2.6 mmol) in CH_2Cl_2 (5 mL) at −60 °C and then at 20 °C for 4 h provided 240 mg (49%) of **5**; 140 mg (31%) of **bis[1-methyl-2-(3,4-dimethoxyphenyl)ethyl] ether (14)** as a 1:1 mixture of diastereomers, mp 38−55 °C. ^1H NMR: 1.00 and 1.11 (d, 6H, ^3J = 6.0 Hz), 2.48 and 2.57 (dd, 2H, ^2J = 13.5 and 13.2 Hz, ^3J = 6.3 and 6.6 Hz, CH_AH_B), 2.72 and 2.77 (dd, 2H, ^3J = 6.3 Hz, CH_AH_B), 3.54 and 3.59 (tq, 2H, $^3J_1 = {}^3J_2$ = 6.3 Hz), 3.84, 3.85, and 3.86 (br s, 12H), 6.62−6.80 (m, 6H). MS (CI/NH_3): 392 $(M + 18)^+$. Anal. Found: C, 70.43; H, 7.84. $C_{22}H_{30}O_5$ requires: C, 70.55; H, 8.09. Further elution with h/ea 1:2 recovered 30 mg (6%) of alcohol **11**.

(c) Treatment of alcohol **12** (980 mg, 5 mmol) with DAST (0.99 mL, 7.5 mmol) at −55 °C for 1 h and then at 25 °C for 18 h and subsequent workup and flash chromatography (h/ea, 3:1 then 1:2) afforded 754 mg (76%) of **1,2-dimethoxy-4-(3-fluoropropyl)benzene (6)** (98% purity). ^1H NMR: 1.99 (dm, 2H, $^3J_{HF}$ = 25.2 Hz), 2.70 (t, 2H, J = 7.5 Hz), 3.86, 3.88 (s, 3H), 4.46 (dt, 2H, $^2J_{HF}$ = 47.1, $^3J_{HH}$ = 5.8 Hz), 6.71−6.83 (m, 3H). ^{19}F NMR: −220.8 (tt). MS (EI): M^+ 198 (44), 151 (100). Anal. Found: C, 66.28; H, 7.62. $C_{11}H_{15}FO_2$ requires: C, 66.63; H,7.64. Second fraction: 107 mg (11%) of **12**.

(d) Treatment of alcohol **12** (359 mg, 1.83 mmol) in CH_2Cl_2 (5 mL) with DAST (256 μL, 1.94 mmol) at −45 °C, warming of the reaction mixture to −30 °C, and subsequent workup with ice-cold saturated $NaHCO_3$ solution followed by extraction ($CHCl_3$) and flash chromatography (h/ea, 3:2) afforded 68 mg (19%) of **6**, 173 mg (30%) of **3,4-dimethoxybenzenepropanol diethylamidosulfite (18)** [R_f 0.35 (h/ea, 3:2). ^1H NMR: 1.59 (t, 6H, J = 7.2 Hz), 1.94 (m, 2H), 2.65 (t, 2H, J = 7.2 Hz), 3.20

(35) Sodium dithionite (ref 33) mainly led to isomerization of the double bond and RMgX/Ni(acac) (ref 34) gave predominantly substitution products.

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(m, 4H), 3.78 (m, 2H), 3.86 and 3.87 (s, 3H), 6.65–6.82 (m, 3H). MS (CI/NH_3): 333 $(M + 18)^+$. Anal. Found: C, 56.80; H, 7.85. $C_{15}H_{25}NO_4S$ requires: C, 57.11; H, 8.00], and a third fraction, 70 mg (20%) of **bis[3-(3,4-dimethoxyphenyl)propyl] carbonate (15)** [R_f 0.27 (h/ea, 3:2). ^1H NMR: 2.0 (tt, 4H), 2.67 (t, 4H, J = 7.2 Hz), 3.85 and 3.87 (s, 6H), 4.16 (t, 4H, J = 6.6 Hz), 6.60–6.85 (m, 6H). IR (neat): 1740 cm^{-1}. MS (CI/NH_3): 436 $(M + 18)^+$. Anal. Found: C, 65.67; H, 7.10. $C_{23}H_{30}O_7$ requires: C, 66.00; H, 7.24]. Elution with h/ea, 1:2, recovered 51 mg (19%) of starting alcohol **12**.

(e) Reaction of alcohol **13** (911 mg, 5 mmol) with DAST (1.0 mL, 7.5 mmol) was carried out as described in procedure **a** and continued at 25 °C for 2.0 h. Distillation of the crude product provided 800 mg of fluoride **7** (bp 85–86 °C/0.3 mm) that was dissolved in hexane (50–60 mL), washed with water, dried, and redistilled to furnish 737 mg (80%) of **1,2-dimethoxy-4-(2-fluoroethyl)benzene (7)**, bp 83–84 °C/0.3 mm (98% purity). ^1H NMR: 2.96 (dt, 2H, $^3J_{HF}$ = 23.1, $^3J_{HH}$ = 6.6 Hz), 3.86, and 3.88 (s, 3H), 4.61 (dt, 2H, $^2J_{HF}$ = 46.8 Hz), 6.76 (br s, 1H), 6.78 (dd, 1H), 6.82 (d, 1H). ^{19}F NMR: −215.6 (tt). MS (EI): M^+ 184 (51), 151 (100). Anal. Found: C, 65.34; H, 7.16. $C_{10}H_{13}FO_2$ requires: C, 65.19; H,7.13.

(f) Reaction of alcohol **13** (1.822 g, 10 mmol) with DAST (1.58 mL, 12 mmol) and subsequent isolation of the products, carried out according to procedure **d**, afforded 1.12 g (37%) of **3,4-dimethoxybenzeneethanol diethylamidosulfite (19)** [R_f 0.47 (h/ea, 1:1). ^1H NMR: 1.12 (t, 6H, J = 7.2 Hz), 2.89 (t, 2H, J = 6.9 Hz), 3.17 (AB part of ABX_3, NCH_2CH_3, $^2J_{AB}$ = 15.0 Hz), 3.86 and 3.87 (s, 3H), 3.93 (AB part of ABX_2, OCH_2, $^2J_{AB}$ = 10.2, $^3J_{AX}$ = $^3J_{BX}$ = 7.2 Hz), 6.75–6.83 (m, 3H). MS (CI/NH_3): 319 $(M + 18)^+$. Anal. Found: C, 55.51; H, 7.54. $C_{14}H_{23}NO_4S$ requires: C, 55.78; H, 7.71] and 390 mg (22%) of **bis[(3,4-dimethoxyphenyl)ethyl] carbonate (16)**, mp 95 °C (ethanol) [R_f 0.38 (h/ea, 1:1). ^1H NMR: 2.89 (t, 4H, J = 7.2 Hz), 3.86 and 3.87 (s, 6H), 4.30 (t, 4H), 6.70–6.83 (m, 6H). IR (Nujol): 1735 cm^{-1}. MS (CI/NH_3): 408 $(M + 18)^+$. Anal. Found: C, 64.57; H, 6.79. $C_{21}H_{26}O_7$ requires: C, 64.59; H, 6.72]. Starting alcohol **13** and fluoride **7** were not isolated.

1,2-Dimethoxy-4-(2-fluoro-3-iodopropyl)benzene (20). Tetrafluoroboric acid (4.16 mL, 24 mmol, 85% diethyl ether complex) was added to a solution of bis(pyridine)iodonium tetrafluoroborate[18] (4.44 g, 12 mmol) in CH_2Cl_2 (65 mL) at −60 °C. After the mixture was stirred for 15 min, a solution of **1** (1.78 g, 10 mmol) in CH_2Cl_2 (25 mL) was added during 1 h at −70 °C. The mixture was stirred for an additional 1 h at −70 °C, poured into 5% solution of $NaHCO_3$ (100 mL), and extracted with CH_2Cl_2. The extract was washed with 0.1 M HCl, 5% $NaHCO_3$, 0.1 N $Na_2S_2O_3$, and water and then dried (Na_2SO_4) and concentrated. Flash chromatography (h/ea, 4:1) afforded 2.03 g (63%) of fluoro iodide 20 (97% purity). ^1H NMR: 3.03 (dd, 2H, $^3J_{HF}$ = 20.8, $^3J_{HH}$ = 5.8 Hz), 3.27 (m, 2H), 3.86, 3.88 (s, 3H), 4.63 (dtt, 1H, $^2J_{HF}$ = 46.8 Hz), 6.77–6.84 (m, 3H). ^{19}F NMR: −168.7 (dtt). MS (EI): M^+ 324 (100), 151 (85). Anal. Found: C, 40.77; H, 4.35. $C_{11}H_{14}FIO_2$ requires: C, 40.76; H, 4.36.

1,2-Dimethoxy-4-(2-fluoro-2-propenyl)benzene (4). Fluoro iodide **20** (4.60 g, 14.2 mmol) was refluxed with DBU (4.26 mL, 28.4 mmol) in benzene (46 mL) for 5–6 h until completion of elimination (TLC). The mixture was poured into water and extracted with benzene. The benzene extract was washed with 10% HCl and water and then was dried and concentrated *in vacuo*. Distillation of the residue afforded 2.18 g (78%) of fluoride **4** (98%), bp 86 °C/0.25 mm. ^1H NMR: 3.45 (d, 2H, $^3J_{HF}$ = 15 Hz), 3.87, 3.88 (s, 3H), 4.25 (dd, 1H, $^3J_{HF}$ = 49.0, $^2J_{HH}$ = 2.7 Hz), 4.60 (dd, 1H, $^3J_{HF}$ = 16.8 Hz), 6.76–6.85 (m, 3H). ^{19}F NMR: −94.9 (m). MS (EI): M^+ 196 (100), 181 (20). Anal. Found: C, 67.11; H, 6.72. $C_{11}H_{13}FO_2$ requires: C, 67.32; H, 6.69.

***(Z)*-1,2-Dimethoxy-4-(3-fluoro-2-propenyl)benzene (2).** Trichlorofluoromethane (193 μL, 2.1 mmol) was added to a solution of tri-*n*-butylphosphine (1.57 mL, 6.3 mmol, Sigma) in CH_2Cl_2 (2 mL) at 0 °C.

The mixture was stirred at 0 °C for 1 h and then at 25 °C for 3 h. To the resultant solution was added aldehyde **21** (320 mg, 1.78 mmol) in CH_2Cl_2 (2 mL) at 0 °C. The mixture was stirred at 0 °C for 1 h and then at 25 °C for 18 h. A solution of 10% NaOH (2.67 mL) was added at once, whereupon the temperature rose to 35 °C. Stirring was continued for 1.5 h, and the mixture was poured into ice–water followed by extraction with CH_2Cl_2, washing of the extract with 10% HCl, 40% $NaHSO_3$, and water, and drying.

Evaporation of the solvent and flash chromatography (h/ea, 4:1) afforded 200 mg (57%) of **2**, *Z*:*E* = 97:3 (GC). ^1H NMR: 3.41 (br d, 2H, J = 7.8 Hz), 3.86, 3.88 (s, 3H), 4.88 (dtd, 1H, $^3J_{HF}$ = 41.7, $^3J_{cis}$ = 4.6 Hz), 6.56 (ddt, 1H, $^2J_{HF}$ = 85.2, $^4J_{HH}$ = 1.3 Hz), 6.72–6.83 (m, 3H). ^{19}F NMR: −131.9 (dd). MS (EI): M^+196 (100), 181 (15), 165 (28).

***(Z)*- and *(E)*-1,2-Dimethoxy-4-[3-fluoro-3-(phenylsulfonyl)-2-propenyl]benzenes (24).** **(a)** To a solution of fluoromethyl phenyl sulfone[23] (490 mg, 2.82 mmol) in THF (7mL) was added a THF complex of LDA (3.38 mL, 1.5 M in cyclohexane, 5.08 mmol) at −60 °C. After 15 min, diethyl chlorophosphate (408 μL, 2.82 mmol) was added and the mixture was stirred for 1 h at −60 to −65 °C. A solution of aldehyde **21** (338 mg, 1.88 mmol) in THF (3 mL) was added, maintaining the temperature at −55 to −60 °C. The cooling bath was removed, and the mixture was allowed to warm to −40 °C and, after 1 h of stirring at this temperature, was poured into an ice-cooled solution of NH_4Cl. The products were extracted with ethyl acetate, and the extract was washed with a solution of NH_4Cl and dried. Evaporation of the solvent and flash chromatography (h/ea, 2:1) provided 610 mg (97%) of sulfone **24** as a 3:2 mixture of *(E)*- and *(Z)*-isomers. Recrystallization of a 2.18 g mixture from 10 mL of ethanol afforded 610 mg of product, *Z*/*E* = 85:15. Further crystallization from 3 mL of ethanol gave 432 mg of colorless needles, *Z*/*E* = 93:7, mp 104 °C. ^1H NMR (**24**-(*Z*)): 3.86, 3.87 (s, 3H), 3.95 (d, 2H, J = 8.7 Hz), 6.0 (dt, 1H, $^3J_{HF}$ = 21.3, $^3J_{HH}$ = 8.7 Hz), 6.73–6.78 (m, 2H), 6.81 (d, 1H), 7.55–8.03 (m, 5H). ^{19}F NMR: −116.4 (d). Anal. Found: C, 60.30; H, 5.22. $C_{17}H_{17}FO_4S$ requires: C, 60.69; H, 5.10. Evaporation of mother liquor from the first crystallization gave 1.57 g of oil which solidified in a freezer. Recrystallization of that product from 5 mL of ethanol gave 992 mg of yellow crystals, *E*/*Z* = 92:8, mp 65 °C. ^1H NMR (**24**-(*E*)): 3.44 (dd, 2H, $^3J_{HH}$ = 7.8, $^4J_{HF}$ = 2.1 Hz), 3.82, 3.86 (s, 3H), 6.43 (dt, 1H, $^3J_{HF}$ = 31.5, $^3J_{HH}$ = 7.8 Hz), 6.62 (d, 1H, J = 1.8 Hz), 6.69 (dd, 1H, J = 8.1 and 1.8 Hz), 6.80 (d, 1H), 7.55–8.0 (m, 5H). ^{19}F NMR: −129.0 (br d). Anal. Found: C, 60.42; H, 5.27. $C_{17}H_{17}FO_4S$ requires: C, 60.69; H, 5.10. Further crystallization did not increase the geometrical purity of either isomer.

(b) The reaction was conducted as described in **a** and after addition of aldehyde **21**, the mixture was warmed to 25 °C and stirred for 5 h. Regular workup and flash chromatography (h/ea, 3:2) afforded 340 mg of a 3:2 mixture of **24**-(*E*) and **24**-(*Z*) and 270 mg of **(*E*)-1,2-dimethoxy-4-[3-fluoro-3-(phenylsulfonyl)-1-propenyl]benzene (25)**, mp 87 °C (h/ea, 2:1). ^1H NMR: 3.90 (s, 6H), 5.67 (dd, 1H, $^2J_{HF}$ = 47.0, $^3J_{HH}$ = 6.9 Hz), 6.10 (ddd, 1H, $^3J_{HF}$ = 13.8, $^3J_{HH}$ = 16.2 Hz), 6.80 (dd, 1H, $^4J_{HF}$ = 2.5 Hz), 6.84 (d, 1H, J = 8.1 Hz), 6.94 (s, 1H), 6.95 (d,1H), 7.55–8.0 (m, 5H). ^{19}F NMR: −171.4 (dd). Anal. Found: C, 60.37; H, 5.28. $C_{17}H_{17}FO_4S$ requires: C, 60.69; H, 5.10.

[1-Fluoro-3-(3,4-dimethoxyphenyl)-1-propenyl]tributylstannane (26). Tributyltin hydride (538 μL, 2 mmol) was added to a solution of sulfone **24**-(*Z*) (336 mg, 1 mmol) and AIBN (14 mg) in toluene (10 mL). The mixture was heated at 78–82 °C for 3–4 h until completion of the reaction (by TLC). Evaporation of the toluene and flash chromatography gave 391 mg (81%) of **26**, *E*/*Z* = 76:24 (NMR). ^1H NMR: 0.89 (t, 9H), 1.0 (m, CH_2Sn, *E*), 1.07(m, CH_2Sn, *Z*), 1.33 (tq, 6H), 1.53 (m, 6H), 3.19 (br d, ^3J = 8.4 Hz, CH_2-ar, *Z*), 3.47 (br d, ^3J = 7.3 Hz, CH_2-ar, *E*), 3.86, 3.87 (s, 3H), 4.99 (dt, $^3J_{HF}$ = 53.0, $^3J_{HH}$ = 7.5 Hz, CH=CF, *E*), 6.03 (dt, $^3J_{HF}$ = 36.0, $^3J_{HH}$ = 8.4 Hz, CH=CF, *Z*), 6.70–6.83 (m, 3H). ^{19}F NMR: −98.3 (d, $^3J_{FH}$ = 37.3 Hz, *Z*), −104.5 (d, $^3J_{FH}$ = 52.3 Hz, *E*). MS (CI/NH_3): 504 $(M + 18)^+$, 521 $(M + 35)^+$. Anal. Found: C, 56.64; H, 7.90. $C_{23}H_{39}FO_2Sn$ requires: C, 56.92; H, 8.12.

Analoguosly **24**-(*E*) afforded a 75% yield of **26**, *E*/*Z* = 75:25.

Destannylation of (Fluorovinyl)stannane 26. Stannane **23** (280 mg, 0.58 mmol) was stirred with tetrabutylammonium fluoride (0.85 mL, 1 M in THF, 0.85 mmol) in THF (5 mL) at 25 °C for 2 h. After completion of the reaction (by TLC), 1:1

ether/hexane (15 mL) was added, and the mixture was washed with water, dried, and concentrated. Flash chromatography (h/ea, 4:1) gave 85 mg (75%) of a 4:1 mixture of **2** and **3**.

Reduction of Fluorovinyl Sulfones 24 with Sodium Amalgam. Sulfone **24** (1 equiv) was dissolved in an 8:1 mixture of MeOH and THF (2.5 mL/0.1 mmol), and Na_2HPO_4 (7.2 equiv) followed by pulverized sodium amalgam (2% Na, 6 equiv) was added at the temperature specified in Table 1. After stirring for the indicated time, the mixture was filtered, neutralized with 10% HCl, evaporated, and extracted with ether. The extract was dried and analyzed by GC-MS (Table 1). The reduction products of **24**-(*Z*) (entry 4) were chromatographed on $AgNO_3$–SiO_2 (10% $AgNO_3$, h/ea, 25:1) to provide 70% yield of **3**, *E*/*Z* = 85:15. ^{1}H NMR (**3**): 3.20 (br d, 2H, J = 7.8 Hz), 3.87, 3.88 (s, 3H), 5.53 (ddt, 1H, $^3J_{HF}$ = 18.3, $^3J_{trans}$ = 11.1 Hz), 6.57 (ddt, 1H, $^2J_{HF}$ = 84.8, $^4J_{HH}$ = 1.2 Hz), 6.68–6.84 (m, 3H). ^{19}F NMR: −129.9 (dd). MS (EI): M^+ 196 (100), 181 (15), 165 (34). Anal. Found: C, 67.39; H, 6.66. $C_{11}H_{13}FO_2$ requires: C, 67.32; H, 6.69. Reduction of a 3:2 mixture of **24**-(*E*) and **24**-(*Z*) at −20 °C (entry 2) afforded a 69% yield of a 1.6:1 mixture of **3** and **2**.

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