Regioselective Synthesis of 6-[Chloro(difluoro)methyl]salicylates by [3 + 3] Cyclocondensations of 1,3-Bis(trimethylsilyloxy)buta-1,3-dienes with 1-Chloro-1,1-difluoro-4-(trimethylsilyloxy)pent-3-en-2-one

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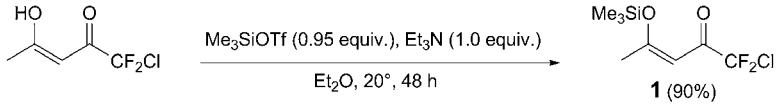
The $TiCl_4$-mediated [3 + 3] cyclocondensation of various 1,3-bis(trimethylsilyloxy)buta-1,3-dienes with 1-chloro-1,1-difluoro-4-(trimethylsilyloxy)pent-3-en-2-one provides a regioselective access to novel 6-(chlorodifluoromethyl)salicylates (= 6-(chlorodifluoromethyl)-2-hydroxybenzoates) with very good regioselectivity. For selected products, it was demonstrated that the CF_2Cl group can be transformed to CF_2H and CF_2(Allyl) by free-radical reactions.

Introduction. – [Chloro(difluoro)methyl]-substituted arenes are of considerable interest in medicinal chemistry, for example, as tyrosine kinase inhibitors [1][2]. They have been prepared by reaction of arenes with bis[chloro(difluoro)acetyl] peroxide [3], by UV-mediated reaction of difluoromethyl arenes with Cl_2 [4], by reaction of (ethylsulfanyl)difluoromethyl arenes with BrF_3 [5], and by fluorination of trichloromethyl arenes (using *Olah*'s reagent or KF in ionic liquids) [6]. All these methods rely on the fluorination or chlorination of suitable benzene derivatives. Despite their utility, they have severe drawbacks with regard to their preparative scope. In addition, some halogenation reagents are toxic and/or very expensive. In addition, the starting materials, *i.e.*, functionalized benzene derivatives, are not readily available. An alternative way for the synthesis of halogenated arenes relies on a 'building block' approach. *Chan* and *Brownbridge* were the first to report [7] a convenient synthesis of functionalized salicylates by $TiCl_4$-mediated [3 + 3] cyclization [8] of 1,3-bis(trimethylsilyloxy)buta-1,3-dienes [9] with 3-alkoxy- and 3-(silyloxy)-alk-2-en-1-ones. We have reported the application of this methodology to the synthesis of CF_3-substituted arenes [10]. Here, we report a new synthesis of 6-[chloro(difluoro)methyl]salicylates (= 6-[chloro(difluoro)methyl]-2-hydroxybenzoates) by regioselective [3 + 3] cyclocondensation of various 1,3-bis(trimethylsilyloxy)buta-1,3-dienes with alkyl- and aryl-substituted 1-chloro-1,1-difluoro-4-(trimethylsilyloxy)pent-3-en-2-ones. The novel products reported in this work are formed with very good regioselectivity, and they are not readily available by other methods.

Results and Discussion. – 1-Chloro-1,1-difluoro-4-(trimethylsilyloxy)pent-3-en-2-one (**1**) was prepared by silylation of known 1-chloro-1,1-difluoro-4-hydroxypent-3-en-

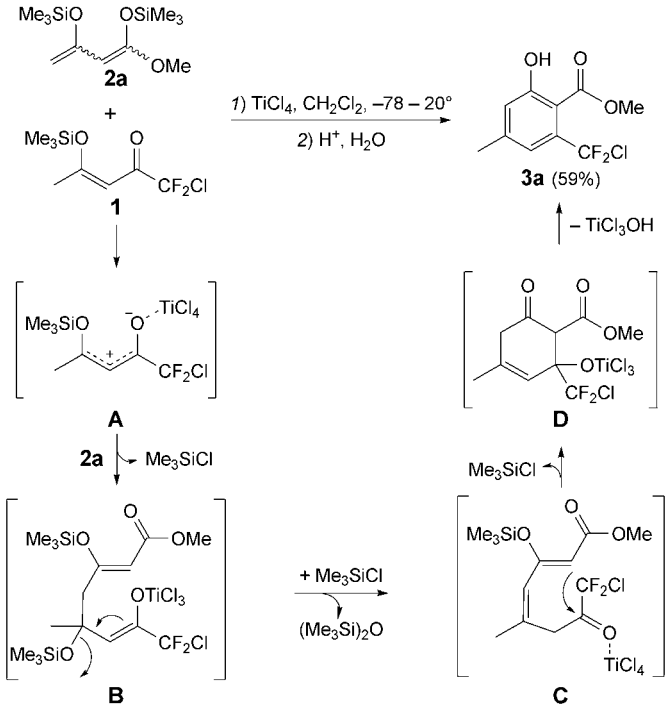
2-one (*Scheme 1*). The latter was obtained from the NaH-mediated reaction of acetone with methyl 2-chloro-2,2-difluoroacetate. 1,3-Bis(trimethylsilyloxy)buta-1,3-dienes **2a**–**2y** were prepared in two steps from the corresponding β-keto esters [7][11][12].

Scheme 1. *Synthesis of* **1**



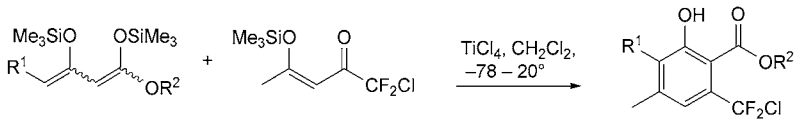
The $TiCl_4$-mediated reaction of **1** with 4-methoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**2a**) afforded 6-[chloro(difluoro)methyl]-4-methylsalicylate (**3a**) in 59% yield (*Scheme 2*). The formation of **3a** can be explained, in analogy to the synthesis of the corresponding CF_3-substituted analogs [10], by the mechanism depicted in *Scheme 2:* the reaction of **1** with $TiCl_4$ affords allylic cation **A**. The reaction of the latter with the terminal C-atom of **2a** gives intermediate **B**. The latter undergoes a cyclization *via* intermediate **C** to afford **D**, which is finally transformed to the product by aromatization (before or during the aqueous workup).

Scheme 2. *Mechanism Proposed for the Formation of* **3a**



The $TiCl_4$-mediated reaction of **1** with 1,3-bis(trimethylsilyloxy)buta-1,3-dienes **2a**–**2y** afforded the 6-(chlorodifluoromethyl)-4-methylsalicylates **3a**–**3y** in 34–81%

Table 1. *Synthesis of* **3a** – **3y**



2a – 2y **1** **3a – 3y**

Pruduct	R^1	R^2	Yield [%][a])
3a	H	Me	59
3b	H	Me_2CH	41
3c	H	Me_2CHCH_2	45
3d	H	$Me_2CHCH_2CH_2$	57
3e	H	$Me(CH_2)_6CH_2$	62
3f	Me	Me	81
3g	Et	Me	47
3h	Et	Et	52
3i	Pr	Me	54
3j	CH_2=CH – CH_2	Me	51
3k	Me_2CH	Et	42
3l	$Me_2CHCH_2CH_2$	Me	59
3m	$Me(CH_2)_3CH_2$	Et	42
3n	$Me(CH_2)_4CH_2$	Et	56
3o	$Me(CH_2)_5CH_2$	Et	55
3p	$Me(CH_2)_6CH_2$	Me	55
3q	$Me(CH_2)_7CH_2$	Me	59
3r	$Me(CH_2)_8CH_2$	Et	34
3s	$Me(CH_2)_{10}CH_2$	Me	62
3t	$Me(CH_2)_{14}CH_2$	Me	41
3u	$Ph(CH_2)_2$	Me	61
3v	4-F–C_6H_4–CH_2	Me	65
3w	Cl	Me	35
3x	$Cl(CH_2)_3$	Me	66
3y	$Cl(CH_2)_4$	Me	62

[a]) Yields of isolated products.

yield (*Table 1*). The yields of most of the products are in the range of 41 – 66%. The yields drop for sterically hindered dienes (*i.e.*, **2k**) and, in case of the Cl-substituted diene **2w**. The purity of each individual diene also plays an important role. In some reactions, the formation of a small amount of β-keto ester from the hydrolysis of the diene was observed. Its chromatographic separation from the product was difficult in some cases. Therefore, practical problems during the chromatographic purification also influenced the yields. During the optimization, the stoichiometry and the concentration played an important role (*Table 2*). The best yield was obtained when **1**, **2a**, and $TiCl_4$ were used in a stoichiometry of 1:2:1 with a concentration of **1** of 0.2M.

All reactions proceeded with very good regioselectivity. The CF_2Cl group is located *ortho* to the ester group. This type of regioselectivity was previously observed for cyclizations of related CF_3-substituted silyl enol ethers [10a]. The structures of various

Table 2. *Optimization of the Synthesis of* **3a**

n(**1**) [mmol]	n(**2a**) [mmol]	n($TiCl_4$) [mmol]	CH_2Cl_2 [ml]	Yield of **3a** [%][a])
1	2	1	1	30
1	2	1	2	29
1	2	1	5	59
1	1	1	10	34

[a]) Yields of isolated product.

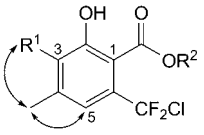


Fig. 1. *NOESY* (H ↔ H) *Correlations for the corroboration of the structure of* **3**

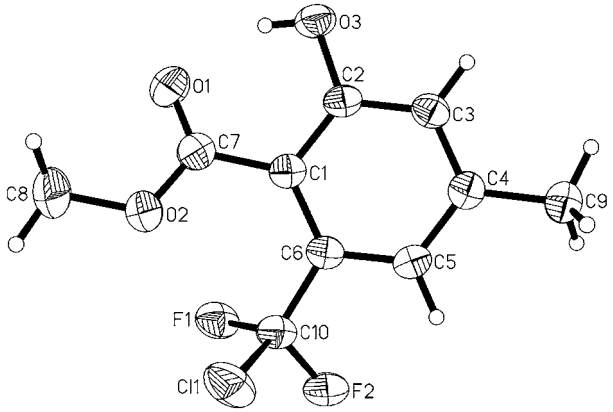


Fig. 2. *ORTEP Plot of* **3a** (50% probability level)

products were established by NOESY experiments (*Fig. 1*). The structure of **3a** was independently confirmed by X-ray crystal-structure analysis (*Fig. 2*)[1]).

Conclusions. – In conclusion, we reported a convenient and regioselective synthesis of 6-[chloro(difluoro)methyl]-4-methylsalicylates by $TiCl_4$-mediated [3 + 3] cyclocondensation of 1,3-bis(trimethylsilyloxy)buta-1,3-dienes with 1-chloro-1,1-difluoro-4-(trimethylsilyloxy)pent-3-en-2-one.

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[1]) CCDC-865454 contains all crystallographic details of this publication and is available free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or can be ordered from the following address: *Cambridge Crystallographic Data Centre*, 12 Union Road, GB-Cambridge CB21EZ; Fax: (+44)1223-336-033; or deposit@ccdc.cam.ac.uk.

Experimental Part

General. CH_2Cl_2 (anh. 99.8%) was purchased directly from *ACROS* and used without further purification. $TiCl_4$ was purchased from *Aldrich*. All cyclization reactions were carried out in *Schlenk* tubes under Ar using dried solvents. Column chromatography (CC): *60 A* silica gel (SiO_2, 60–200 mesh). Anal. TLC: 0.20 mm *60 A* SiO_2 plates. M.p.: Microheating table *HMK 67/1825 Kuestner* (*Büchi* apparatus); uncorrected. IR Spectra: FT-IR spectrometer; $\tilde{\nu}$ in cm^{-1}. ^{1}H-NMR Spectra: at 300 and 400 MHz resp.; in $CDCl_3$. ^{13}C-NMR Spectra: at 75 and 100 MHz, resp.; in $CDCl_3$; δ in ppm with the solvent as internal standard ($CHCl_3$, 7.26 and 77.0 ppm, resp.); J in Hz. MS: electron ionization (EI, 70 eV), chemical ionization (CI, isobutane), or electrospray ionization (ESI); in m/z. Crystallographic data were collected on a *STEO IPDS 2* diffractometer with MoK_α radiation ($\lambda = 0.71073$ Å). The structure was solved by direct methods using SHELXS-97 and refined against F^2 on all data by full-matrix least-squares with SHELXL-97. All non-H-atoms were refined anisotropically, and the H-atoms (except H3b) were refined in the model at geometrically calculated positions and refined using a riding model.

General Procedure for the Synthesis of 1-Chloro-1,1-difluoro-4-hydroxypent-3-en-2-one. The synthesis of the title compound has been reported in [13]. To a soln. of NaH (1.1 equiv.) in Et_2O (2.0 ml/mmol reactant) was added acetone (1.0 equiv.) at 0°. The soln. was stirred at 0° for 10 min, before methyl 2-chloro-2,2-difluoroacetate (1.0 equiv.) was added. The temp. was allowed to rise to 20° over 14 h. To the soln. was added HCl (10%), and the mixture was extracted with Et_2O. The org. layers were dried (Na_2SO_4) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified by chromatography (heptane/AcOEt) to give the product.

1,3-Bis(trimethylsilyloxy)buta-1,3-dienes **2a**–**2y** were prepared according to the literature from the corresponding β-keto esters in two steps [7][11][12]. Silyl enol ethers **1** were also prepared in analogy to reported procedures [7].

Procedure for the Synthesis of **3a**–**3y**. To **1** (1.0 equiv.) and **2** (1.0 equiv.) in CH_2Cl_2 (2.0 ml/1 mmol of **1**) was added $TiCl_4$ (1.0 equiv.) at −78°. The soln. was slowly allowed to warm to 20° with stirring. To the soln. was added HCl (10%), and the org. and the aq. layers were separated. The latter was extracted with CH_2Cl_2. The combined org. layers were dried (Na_2SO_4) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified by CC (SiO_2, heptane/AcOEt 30:1).

Methyl 2-[Chloro(difluoro)methyl]-6-hydroxy-4-methylbenzoate (**3a**). *4-(Trimethylsilyloxy)-1-chloro-1,1-difluoropent-3-en-2-one* (**1**; 0.242 g, 1.0 mmol), *1-methoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene* (**2a**; 0.521 g, 2.0 mmol), and $TiCl_4$ (0.1 ml, 1.0 mmol) in CH_2Cl_2 (5 ml) gave **3a** (0.148 g, 59%). Slight yellow solid. M.p. 41–42°. R_f (hexane/CH_2Cl_2 3:2) 0.50. IR (ATR): 3389*w*, 2960*w*, 2866*w*, 2740*w*, 1710*m*, 1619*m*, 1435*m*, 1386*w*, 1326*m*, 1300*s*, 1273*s*, 1119*s*, 1090*s*, 956*s*, 830*s*, 806*s*. ^{1}H-NMR (300 MHz): 2.37 (*s*, Me); 3.96 (*s*, MeO); 6.97 (*s*, H–C(5)); 7.08 (*s*, H–C(3)); 10.31 (*s*, OH). ^{13}C-NMR (75 MHz): 21.7 (Me); 52.5 (MeO); 108.3 (*t*, J(C,F) = 1.9, C(1)); 119.2 (*t*, J(C,F) = 8.8, C(5)); 125.1 (*t*, J(C,F) = 286.4, CF_2Cl); 135.9 (*t*, J(C,F) = 25.8, C(6)); 144.8; 161.1 (C); 169.6 (COO). ^{19}F-NMR (282 MHz): −44.8 (CF_2Cl). GC/MS (EI, 70 eV): 252 (11), 250 (M^+, 33), 220 (35), 219 (22), 218 (100), 215 (10), 195 (17), 180 (10), 155 (80), 127 (11). HR-MS (EI, 70 eV): 250.020617 ($C_{10}H_9ClF_2O_3^+$; calc. 250.02028).

1-Methylethyl 2-[Chloro(difluoro)methyl]-6-hydroxy-4-methylbenzoate (**3b**). Compound **1** (0.242 g, 1.0 mmol), *1-(1-methylethoxy)-1,3-bis(trimethylsilyloxy)buta-1,3-diene* (**2b**; 0.577 g, 2.0 mmol), and $TiCl_4$ (0.1 ml, 1.0 mmol) in CH_2Cl_2 (5 ml), yielded **3b** (0.108 g, 41%). White solid. M.p. 47–48°. R_f (hexane/CH_2Cl_2 3:2) 0.67. IR (ATR): 3184*w*, 3063*w*, 2986*w*, 2936*w*, 2884*w*, 1665*m*, 1619*m*, 1580*w*, 1495*w*, 1453*m*, 1374*m*, 1274*m*, 1217*m*, 1148*m*, 1094*s*, 954*s*, 855*s*, 805*s*, 792*s*. ^{1}H-NMR (300 MHz): 1.40 (*s*, Me); 1.42 (*s*, Me), 2.36 (*s*, Me); 5.26–5.41 (*m*, 2 CH); 6.95 (*s*, CH); 7.06 (*d*, ^4J = 1.5, H–C(5)); 10.56 (*s*, OH). ^{13}C-NMR (100 MHz): 21.4, 21.6 (Me); 71.0 (CH); 108.9 (C(1)); 119.1 (*t*, J(C,F) = 8.8, C(5)); 121.3 (C(3)); 125.1 (*t*, J(C,F) = 290.0, CF_2Cl); 135.8 (*t*, J(C,F) = 25.6, C(6)); 144.5; 161.2 (C); 168.8 (COO). ^{19}F-NMR (282 MHz): −43.9 (CF_2Cl). GC/MS (EI, 70 eV): 278 (M^+, 11), 236 (13), 220 (34), 219 (22), 218 (100), 155 (37). Anal. calc. for $C_{12}H_{13}ClF_2O_3$ (278.68): C 51.72, H 4.70; found: C 51.68, H 4.76.

2-Methylpropyl 2-[Chloro(difluoro)methyl]-6-hydroxy-4-methylbenzoate (**3c**). Compound **1** (0.242 g, 1.0 mmol), *1-(2-methylpropoxy)-1,3-bis(trimethylsilyloxy)buta-1,3-diene* (**2c**; 0.605 g, 2.0 mmol) and $TiCl_4$ (0.1 ml, 1.0 mmol) in CH_2Cl_2 (5 ml) furnished **3c** (0.132 g, 45%). Colorless liquid. R_f (hexane/

CH_2Cl_2 3:2) 0.63. IR (ATR): 3057*w*, 2963*w*, 2877*w*, 1667*m*, 1619*m*, 1577*w*, 1469*m*, 1399*m*, 1324*m*, 1269*s*, 959*s*, 816*m*, 795*s*, 706*m*. ^{1}H-NMR (400 MHz): 1.00, 1.01 (*s*, Me); 2.07–2.20 (*m*, CH); 2.36 (*s*, Me); 4.16 (*d*, ^3J = 6.7, H–C(3)); 6.96 (br. *s*, H–C(5)); 7.08 (*d*, ^4J = 1.5, CH); 10.37 (*s*, OH). ^{13}C-NMR (100 MHz): 19.2; 21.6 (Me); 27.4 (CH); 72.9 (CH_2O); 108.7 (*t*, *J*(C,F) = 1.6, C(1)); 119.1 (*t*, *J*(C,F) = 8.6, C(5)); 121.3 (C(3)); 125.2 (*t*, *J*(C,F) = 290.1, CF_2Cl); 135.7 (*t*, *J*(C,F) = 25.7, C(6)); 144.5; 161.1 (C); 169.5 (COO). ^{19}F-NMR (282 MHz): −44.4 (CF_2Cl). GC/MS (EI, 70 eV): 292 (M^+, 10), 236 (10), 220 (35), 219 (22), 218 (100), 155 (28). Anal. calc. for $C_{13}H_{15}ClF_2O_3$ (292.71): C 53.34, H 5.17; found: C 53.30, H 5.20.

3-Methylbutyl 2-[Chloro(difluoro)methyl]-6-hydroxy-4-methylbenzoate (**3d**). Compound **1** (0.242 g, 1.0 mmol), *1-(3-methylbutoxy)-1,3-bis(trimethylsilyloxy)buta-1,3-diene* (**2d**; 0.633 g, 2.0 mmol), and $TiCl_4$ (0.1 ml, 1.0 mmol) in CH_2Cl_2 (5 ml) gave **3d** (0.174 g, 57%). White solid. M.p. 30–31°. R_f (hexane/CH_2Cl_2 3:2) 0.40. IR (ATR): 3057*w*, 2956*m*, 2925*w*, 2872*w*, 2840*w*, 1660*s*, 1620*m*, 1581*m*, 1496*w*, 1452*m*, 1324*s*, 1099*s*, 956*s*, 944*s*, 795*s*, 702*s*. ^{1}H-NMR (300 MHz): 0.94 (*s*, Me); 0.96 (*s*, Me); 1.65–1.87 (*m*, $(CH_2)CH$); 2.37 (*s*, Me); 4.40 (*t*, ^3J = 6.9, CH_2O); 6.96 (*d*, ^4J = 0.6, CH); 7.07 (*d*, ^4J = 1.3, CH); 10.44 (*s*, OH). ^{13}C-NMR (75 MHz): 21.6; 22.3 (Me); 24.8 (CH); 36.7 (CH_2); 65.2 (CH_2O); 108.2 (*t*, *J*(C,F) = 1.9, C(1)); 119.1 (*t*, *J*(C,F) = 8.7, C(5)); 125.1 (*t*, *J*(C,F) = 289.1, CF_2Cl); 135.8 (*t*, *J*(C,F) = 25.8, C(6)); 144.6; 161.1 (C); 169.4 (COO). ^{19}F-NMR (282 MHz): −44.4 (CF_2Cl). GC/MS (EI, 70 eV): 306 (M^+, 12), 220 (34), 219 (22), 218 (100), 155 (27), 71 (13), 70 (21), 43 (17). Anal. calc. for $C_{14}H_{17}ClF_2O_3$ (306.73): C 54.82, H 5.59; found: C 54.82, H 5.61.

Octyl 2-[Chloro(difluoro)methyl]-6-hydroxy-4-methylbenzoate (**3e**). Compound **1** (0.242 g, 1.0 mmol), *1-(octyloxy)-1,3-bis(trimethylsilyloxy)buta-1,3-diene* (**2e**; 0.717 g, 2.0 mmol), and $TiCl_4$ (0.1 ml, 1.0 mmol) in CH_2Cl_2 (5 ml) gave **3e** (0.215 g, 62%). Colorless oil. R_f (hexane/CH_2Cl_2 3:2) 0.47. IR (ATR): 2956*m*, 2926*m*, 2856*m*, 1668*m*, 1665*m*, 1620*m*, 1577*w*, 1456 *m*, 1395*m*, 1327*m*, 1270*s*, 1146*m*, 1099*m*, 962*s*, 797*s*. ^{1}H-NMR (300 MHz): 0.88 (*t*, ^3J = 6.8, Me); 1.28–1.43 (*m*, $Me(CH_2)_5$); 2.36 (*s*, Me); 1.75–1.84 (*m*, CH_2); 2.37 (*s*, Me); 4.36 (*t*, ^3J = 6.8, CH_2); 6.96 (*s*, CH); 7.07 (*d*, ^4J = 1.6, CH); 10.45 (*s*, OH). ^{13}C-NMR (75 MHz): 14.1; 21.7 (Me); 22.6, 25.8, 28.1, 29.1, 29.1, 31.7, 66.7 (CH_2); 19.8 (Me); 62.4 (CH_2); 108.5 (t, *J*(C,F) = 1.9, C(1)); 119.1 (*t*, *J*(C,F) = 8.7, C(5)); 125.1 (*t*, *J*(C,F) = 289.1, CF_2Cl); 135.8 (*t*, *J*(C,F) = 25.7, C(6)); 144.6; 161.2.0 (C); 169.4 (COO). ^{19}F-NMR (282 MHz): −44.4 (CF_2Cl). GC/MS (EI, 70 eV): 348 (M^+, 10), 236 (12), 220 (33), 219 (20), 218 (100), 155 (20). Anal. calc. for $C_{17}H_{23}ClF_2O_3$ (348.81): C 58.54, H 6.65; found: C 58.74, H 6.57.

Methyl 6-[Chloro(difluoro)methyl]-2-hydroxy-3,4-dimethylbenzoate (**3f**). Compound **1** (0.242 g, 1.0 mmol), *1-methoxy-1,3-bis(trimethylsilyloxy)penta-1,3-diene* (**2f**; 0.549 g, 2.0 mmol), and $TiCl_4$ (0.1 ml, 1.0 mmol) in CH_2Cl_2 (5 ml) yielded (**3f**) (0.216 g, 81%). Slight yellow oil. R_f (heptane/AcOEt 3:2) 0.72. IR (ATR): 3349*w*, 3043*w*, 3014*w*, 2986*w*, 2960*w*, 2929*w*, 2861*w*, 1703*s*, 1608*m*, 1570*w*, 1492*w*, 1435*m*, 1283*s*, 1236*s*, 1196*m*, 1119*s*, 998*s*, 969*s*, 859*s*, 807*s*, 795*s*, 711*m*. ^{1}H-NMR (300 MHz): 2.21 (*s*, Me); 2.33 (*s*, Me); 3.96 (*s*, MeO); 7.08 (*s*, H–C(5)); 10.61 (*s*, OH). ^{13}C-NMR (75 MHz): 12.0; 20.6 (Me); 52.5 (MeO); 107.9 (*t*, *J*(C,F) = 2.3, C(1)); 119.3 (*t*, *J*(C,F) = 8.3, C(5)); 125.4 (*t*, *J*(C,F) = 288.0, CF_2Cl); 132.7 (*t*, *J*(C,F) = 25.5, C(6)); 129.3; 142.7; 159.1 (C); 170.3 (COO). ^{19}F-NMR (282 MHz): −44.4 (CF_2Cl). GC/MS (EI, 70 eV): 264 (M^+, 37), 234 (17), 233 (19), 232 (48), 214 (34), 213 (17), 212 (100), 209 (19), 196 (52), 169 (22), 141 (10). Anal. calc. for $C_{11}H_{11}ClF_2O_3$ (264.04): C 49.92, H 4.19; found: C 49.96, H 4.23.

Methyl 6-[Chloro(difluoro)methyl]-3-ethyl-2-hydroxy-4-methylbenzoate (**3g**). Compound **1**; 0.242 g, 1.0 mmol), *1-methoxy-1,3-bis(trimethylsilyloxy)hexa-1,3-diene* (**2g**; 0.577 g, 2.0 mmol), and $TiCl_4$ (0.1 ml, 1.0 mmol) in CH_2Cl_2 (5.0 ml) afforded **3g** (0.130 g, 47%). Colorless oil. R_f (hexane/CH_2Cl_2 3:2) 0.63. IR (ATR): 3139*w*, 3060*w*, 3040*w*, 3008*w*, 2979*w*, 2957*w*, 2880*w*, 2853*w*, 1668*s*, 1438*s*, 1333*m*, 1286*s*, 1232*m*, 1148*s*, 1102*s*, 978*m*, 962*m*, 950*m*, 865*s*, 804*s*, 766*s*, 657*s*. ^{1}H-NMR (400 MHz): 1.27 (*t*, ^3J = 7.6, Me); 2.36 (*s*, Me); 2.72 (*q*, ^3J = 7.2, CH_2); 3.96 (*s*, MeO); 7.07 (*s*, H–C(5)); 10.54 (*s*, OH). ^{13}C-NMR (100 MHz): 12.7 (Me); 19.8 (Me); 19.8 (CH_2); 52.4 (MeO); 108.2 (*t*, *J*(C,F) = 2.0, C(1)); 119.6 (*t*, *J*(C,F) = 9.0, C(5)); 125.4 (*t*, *J*(C,F) = 288.0, CF_2Cl); 132.8 (*t*, *J*(C,F) = 25.0, C(6)); 143.0; 159.0 (C); 170.3 (COO). ^{19}F-NMR (282 MHz): −44.4 (CF_2Cl). GC/MS (EI, 70 eV): 278 (M^+, 45), 248 (20), 247 (20), 246 (55), 228 (16), 226 (44), 223 (14), 211 (15), 210 (100), 182 (23), 160 (11). Anal. calc. for $C_{12}H_{13}ClF_2O_3$ (278.68): C 51.72, H 4.70; found: C 51.76, H 4.90.

Ethyl 6-[Chloro(difluoro)methyl]-3-ethyl-2-hydroxy-4-methylbenzoate (**3h**). Compound **1** (0.242 g, 1.0 mmol), *1-ethoxy-1,3-bis(trimethylsilyloxy)hexa-1,3-diene* (**2h**; 0.605 g, 2.0 mmol), and $TiCl_4$ (0.1 ml, 1.0 mmol) in CH_2Cl_2 (5 ml) gave **3h** (0.146 g, 52%). Colorless oil. R_f (hexane/CH_2Cl_2 3:2) 0.69. IR

(ATR): 2978*w*, 2936*w*, 2907*w*, 2876*w*, 1665*m*, 1607*w*, 1573*w*, 1457*w*, 1391*m*, 1373*m*, 1279*s*, 1147*s*, 1104*s*, 958*s*, 804*s*. ^{1}H-NMR (300 MHz): 1.12 (*t*, ^3J = 7.5, Me); 1.43 (*t*, ^3J = 7.2, Me); 2.36 (*s*, Me); 2.72 (*q*, ^3J = 7.5, CH_2); 4.44 (*q*, ^3J = 7.2, CH_2); 7.06 (*s*, H–C(5)); 10.67 (*s*, OH). ^{13}C-NMR (75 MHz): 12.6; 13.6 (Me); 19.7 (CH_2); 19.8 (Me); 62.4 (CH_2); 108.3 (*t*, *J*(C,F) = 1.9, C(1)); 119.6 (*t*, *J*(C,F) = 8.8, C(5)); 125.4 (*t*, *J*(C,F) = 289.7, CF_2Cl); 132.7 (*t*, *J*(C,F) = 25.7, C(6)), 134.9; 141.8; 159.0 (C); 169.9 (COO). ^{19}F-NMR (282 MHz): − 43.8 (CF_2Cl). GC/MS (EI, 70 eV): 294 (12), 292 (M^+,37), 248 (20), 247 (19), 246 (53), 228 (15), 226 (41), 211 (13), 210 (100), 209 (16), 189 (10), 182 (18). Anal. calc. for $C_{13}H_{15}ClF_2O_3$ (292.71): C 53.34, H 5.17; found: C 53.33, H 5.09.

Methyl 6-[Chloro(difluoro)methyl]-2-hydroxy-4-methyl-3-propylbenzoate (**3i**). Compound **1** (0.242 g, 1.0 mmol), *1-methoxy-1,3-bis(trimethylsilyloxy)hepta-1,3-diene* (**2i**; 0.605 g, 2.0 mmol), and $TiCl_4$ (0.1 ml, 1.0 mmol) in CH_2Cl_2 (5 ml) afforded **3i** (0.154 g, 54%). White solid. R_f (hexane/CH_2Cl_2 3 :2) 0.58. IR (ATR): 3006*w*, 2960*w*, 2873*w*, 1672*m*, 1607*w*, 1572*w*, 1438*m*, 1391*m*, 1329*m*, 1273*s*, 1145*s*, 1107*s*, 977*s*, 960*s*, 856*s*, 801*s*. ^{1}H-NMR (300 MHz): 0.99 (*t*, ^3J = 7.3, Me); 1.48 – 1.60 (*m*, MeCH_2); 2.35 (*s*, Me); 2.66 (*t*, ^3J = 7.9, ArCH_2); 3.95 (*s*, MeO); 7.06 (*s*, H–C(5)); 10.55 (*s*, OH). ^{13}C-NMR (75 MHz): 14.4; 20.0 (Me); 21.7; 28.5 (CH_2); 52.4 (MeO); 108.7 (*t*, *J*(C,F) = 1.9, C(1)); 119.6 (*t*, *J*(C,F) = 8.8, C(5)); 125.4 (*t*, *J*(C,F) = 289.6, CF_2Cl); 132.7 (*t*, *J*(C,F) = 25.7, C(6)); 133.6, 142.3, 159.1 (C); 170.3 (COO). ^{19}F-NMR (282 MHz): − 44.3 (CF_2Cl). GC/MS (EI, 70 eV): 294 (23), 293 (10), 292 (M^+,69), 263 (10), 262 (26), 261 (27), 260 (72), 257 (15), 247 (25), 246 (10), 245 (85), 243 (32), 240 (25), 237 (19), 233 (19), 232 (24), 231 (51), 225 (30), 224 (100), 214 (21), 213 (10), 212 (61), 197 (15), 196 (57), 193 (18), 177 (11), 175 (19), 174 (13), 140 (16). Anal. calc. for $C_{13}H_{15}ClF_2O_3$ (292.71): C 53.34, H 5.17; found: C 53.50, H 5.30.

Methyl 6-[Chloro(difluoro)methyl]-2-hydroxy-4-methyl-3-(prop-2-en-1-yl)benzoate (**3j**). Compound **1** (0.242 g, 1.0 mmol), *1-methoxy-1,3-bis(trimethylsilyloxy)hepta-1,3,6-triene* (**2j**; 0.601 g, 2.0 mmol), and $TiCl_4$ (0.1 ml, 1.0 mmol) in CH_2Cl_2 (5 ml) gave **3j** (0.148 g, 51%). Colorless oil. R_f (hexane/CH_2Cl_2 3 :2) 0.60. IR (ATR): 3080*w*, 3008*w*, 2980*w*, 2955*w*, 2930*w*, 2854*w*, 1672*m*, 1638*w*, 1608*w*, 1572*w*, 1438*m*, 1331*m*, 1273*s*, 1144*s*, 1108*s*, 967*s*, 801*s*. ^{1}H-NMR (300 MHz): 2.35 (*s*, Me); 3.47 (*dt*, ^3J = 6.0, CH_2); 3.96 (*s*, MeO); 4.92 – 5.04 (*m*, CH_2CH); 5.83 – 5.96 (*m*, CH); 7.09 (*s*, H–C(5)); 10.59 (*s*, OH). ^{13}C-NMR (75 MHz): 19.9 (Me); 30.5 (CH_2); 52.5 (MeO); 108.3 (*t*, *J*(C,F) = 1.9, C(1)); 115.4 (CH_2); 119.6 (*t*, *J*(C,F) = 8.7, C(5)); 125.2 (*t*, *J*(C,F) = 289.7, CF_2Cl); 130.4 (C(3)); 133.4 (*t*, *J*(C,F) = 25.8, C(6)); 134.2 (CH); 143.1; 158.9 (C); 170.2 (O–CO). ^{19}F-NMR (282 MHz): − 44.5 (CF_2Cl). GC/MS (EI, 70 eV): 292 (19), 290 (M^+, 56), 261 (10), 260 (24), 259 (33), 258 (65), 255 (27), 254 (10), 245 (33), 244 (12), 243 (100), 239 (15), 238 (17), 235 (18), 230 (17), 224 (10), 223 (69), 222 (16), 220 (15), 219 (29), 217 (11), 215 (35), 211 (10), 210 (11), 205 (15), 195 (30), 194 (25), 180 (10), 175 (25), 151 (18), 147 (13), 146 (17), 145 (10), 133 (10), 127 (13), 115 (22). Anal. calc. for $C_{13}H_{13}ClF_2O_3$ (290.69): C 53.71, H 4.51; found: C 53.60, H 4.55.

Ethyl 6-[Chloro(difluoro)methyl]-2-hydroxy-4-methyl-3-(1-methylethyl)benzoate (**3k**). Compound **1** (0.242 g, 1.0 mmol), *1-ethoxy-1,3-bis(trimethylsilyloxy)-5-methylhexa-1,3-diene* (**2k**; 0.633 g, 2.0 mmol), and $TiCl_4$ (0.1 ml, 1.0 mmol) in CH_2Cl_2 (5 ml) provided **3k** (0.128 g, 42%). Colorless liquid. R_f (hexane/CH_2Cl_2 3 :2) 0.67. IR (ATR): 2915*s*, 2848*s*, 1667*w*, 1606*w*, 1468*m*, 1375*w*, 1316*w*, 1265*w*, 718*m*. ^{1}H-NMR (300 MHz): 1.34 (*s*, Me); 1.36 (*s*, Me); 1.42 (*t*, ^3J = 7.2, Me); 2.37 (*s*, Me); 4.43 (*q*, ^3J = 7.1, CH_2); 7.03 (*s*, H–C(5)); 10.59 (*s*, OH). ^{13}C-NMR (75 MHz): 13.6; 19.6; 21.2; 24.1 (Me); 28.7 (CH); 62.4 (CH_2O); 109.1 (*t*, *J*(C,F) = 1.6, C(1)); 120.05 (*t*, *J*(C,F) = 8.6, C(5)); 125.4 (*t*, *J*(C,F) = 289.6, CF_2Cl); 132.7 (*t*, *J*(C,F) = 25.7, C(6)); 137.7; 141.4; 159.9 (C); 169.9 (COO). ^{19}F-NMR (282 MHz): − 43.8 (CF_2Cl). GC/MS (EI, 70 eV): 308 (13), 306 (M^+, 38), 262 (17), 261 (19), 260 (48), 247 (13), 245 (44), 243 (18), 240 (23), 225 (27), 224 (100), 223 (18), 212 (22), 197 (13), 196 (26), 133 (13). Anal. calc. for $C_{14}H_{17}ClF_2O_3$ (306.73): C 54.82, H 5.59; found: C 54.83, H 5.59.

Methyl 6-[Chloro(difluoro)methyl]-2-hydroxy-4-methyl-3-(3-methylbutyl)benzoate (**3l**). Compound **1** (0.242 g, 1.0 mmol), *1-methoxy-1,3-bis(trimethylsilyloxy)-7-methylocta-1,3-diene* (**2l**; 0.661 g, 2.0 mmol), and $TiCl_4$ (0.1 ml, 1.0 mmol) in CH_2Cl_2 (5 ml) afforded **3l** (0.189 g, 59%). Colorless oil. R_f (hexane/CH_2Cl_2 3 :2) 0.78. IR (ATR): 2955*w*, 2870*w*, 1673*m*, 1607*w*, 1572*w*, 1438*m*, 1384*m*, 1269*s*, 1145*s*, 1109*s*, 972 *s*, 802*s*. ^{1}H-NMR (300 MHz): 0.96 (*s*, Me); 0.98 (*s*, Me); 1.31 – 1.38 (*m*, CH_2); 1.60 – 1.73 (*m*, CH); 2.35 (*s*, Me); 2.64 – 2.69 (*m*, ArCH_2); 3.96 (*s*, MeO); 7.06 (*s*, H–C(5)); 10.53 (*s*, OH). ^{13}C-NMR (75 MHz): 19.9; 22.4 (Me); 24.5 (CH_2); 28.6 (CH); 37.4 (CH_2); 52.4 (MeO); 108.1 (*t*, *J*(C,F) = 1.9, C(1)); 119.6 (*t*, *J*(C,F) = 8.7, C(5)); 125.4 (*t*, *J*(C,F) = 289.6, CF_2Cl); 132.7 (*t*, *J*(C,F) = 25.7, C(6)); 134.1, 142.1,

159.0 (C); 170.3 (COO). ^{19}F-NMR (282 MHz): −44.3 (CF_2Cl). GC/MS (EI, 70 eV): 322 (13), 320 (M^+, 37), 289 (11), 288 (11), 285 (11), 273 (19), 234 (34), 233 (24), 232 (100), 231 (31), 214 (32), 213 (11), 212 (95), 208 (14), 197 (10), 196 (34), 193 (15). Anal. calc. for $C_{15}H_{19}ClF_2O_3$ (320.76): C 56.17, H 5.97; found: C 56.12, H 5.83.

Ethyl 6-[Chloro(difluoro)methyl]-2-hydroxy-4-methyl-3-pentylbenzoate (**3m**). Compound **1** (0.242 g, 1.0 mmol), *1-ethoxy-1,3-bis(trimethylsilyloxy)nona-1,3-diene* (**2m**; 0.680 g, 2.0 mmol), and $TiCl_4$ (0.1 ml, 1.0 mmol) in CH_2Cl_2 (5.0 ml) furnished **3m** (0.137 g, 42%). Colorless oil. R_f (hexane/CH_2Cl_2 3:2) 0.19. IR (ATR): 2958*w*, 2929*w*, 2872*w*, 2860*w*, 1666*m*, 1374*m*, 1324*m*, 1278*s*, 1148*s*, 1109*s*, 987*s*, 961*m*, 912 *m*, 865*m*, 822*m*, 802*s*, 725*w*. ^{1}H-NMR (400 MHz): 0.92 (*t*, ^3J = 7.2, Me); 1.35–1.54 (*m*, 9 H, Me, $Me(CH_2)_4$); 2.35 (*s*, Me); 2.69 (*t*, ^3J = 5.6, CH_2); 4.44 (*q*, ^3J = 7.2, CH_2); 7.06 (*s*, H–C(5)); 10.66 (*s*, OH). ^{13}C-NMR (75 MHz): 13.6, 14.0, 20.0 (Me); 22.7, 26.6, 28.1, 32.1 (CH_2); 62.4 (CH_2O); 108.3 (*t*, *J* = 2.0, C(1)); 119.6 (*t*, *J*(C,F) = 8.0, C(5)); 125.5 (*t*, *J*(C,F) = 288.0, CF_2Cl); 132.7 (*t*, *J*(C,F) = 26.0, C(6)); 133.9; 142.0; 159.2 (C); 170.0 (COO). ^{19}F-NMR (282 MHz): −43.8 (CF_2Cl). GC/MS (EI, 70 eV): 335 (M^+, 4), 334 (23), 275 (33), 274 (15), 273 (100), 271 (12), 251 (10), 234 (10), 233 (11), 232 (30), 231 (22), 214 (17), 212 (48), 196 (19). Anal. calc. for $C_{16}H_{21}ClF_2O_3$ (334.79): C 57.40, H 6.32; found: C 57.40, H 6.42.

Ethyl 6-[Chloro(difluoro)methyl]-3-hexyl-2-hydroxy-4-methylbenzoate (**3n**). Compound **1** (0.242 g, 1.0 mmol), *1-ethoxy-1,3-bis(trimethylsilyloxy)deca-1,3-diene* (**2n**; 0.717 g, 2.0 mmol), and $TiCl_4$ (0.1 ml, 1.0 mmol) in CH_2Cl_2 (5 ml) gave **3n** (0.186 g, 56%). Colorless liquid. R_f (hexane/CH_2Cl_2 3:2) 0.76. IR (ATR): 2957*w*, 2927*m*, 2858*w*, 1666*m*, 1607*w*, 1465*m*, 1392*m*, 1373*m*, 1273*s*, 1148*s*, 1110*s*, 990*s*, 802*s*. ^{1}H-NMR (300 MHz): 0.87 (*t*, ^3J = 6.9, Me); 1.24–1.38 (*m*, $Me(CH_2)_4$), Me); 2.31 (*s*, Me), 2.62 (*t*, ^3J = 7.3, ArCH_2); 4.28 (*q*, ^3J = 7.1, CH_2); 7.06 (*s*, H–C(5)); 9.30 (*s*, OH). ^{13}C-NMR (75 MHz): 3.7; 13.8; 19.2 (Me); 21.9; 25.9; 28.0; 28.9; 30.9 (CH_2); 61.2 (CH_2O); 117.8 (*t*, *J*(C,F) = 2.5, C(1)); 118.0 (*t*, *J*(C,F) = 6.1, C(5)); 125.5 (*t*, *J*(C,F) = 289.7, CF_2Cl); 129.1 (*t*, *J*(C,F) = 25.5, C(6)); 133.7, 139.1, 151.9 (C), 165.9 (COO). ^{19}F-NMR (282 MHz): −45.0 (CF_2Cl). GC/MS (EI, 70 eV): 348 (M^+, 26), 303 (10), 289 (33), 288 (15), 287 (100), 285 (11), 266 (13), 265 (10), 234 (12), 233 (12), 232 (37), 231 (22), 214 (18), 212 (52), 196 (21). Anal. calc. for $C_{17}H_{23}ClF_2O_3$ (348.81): C 58.54, H 6.65; found: C 58.26, H 6.58.

Ethyl 6-[Chloro(difluoro)methyl]-3-heptyl-2-hydroxy-4-methylbenzoate (**3o**). Compound **1** (0.242 g, 1.0 mmol), *1-ethoxy-1,3-bis(trimethylsilyloxy)undeca-1,3-diene* (**2o**; 0.744 g, 2.0 mmol), and $TiCl_4$ (0.1 ml, 1.0 mmol) in CH_2Cl_2 (5.0 ml) afforded **3o** (0.199 g, 55%). Slightly yellow oil. R_f (hexane/CH_2Cl_2 3:2) 0.77. IR (ATR): 2957*w*, 2926*w*, 2857*w*, 1667*m*, 1608*w*, 1374*m*, 1270*s*, 1232*m*, 1148*s*, 1111*s*, 975*m*, 803*m*. ^{1}H-NMR (300 MHz): 0.92 (*t*, ^3J = 7.3, Me); 1.21–1.5 (*m*, 13 H, Me, $Me(CH_2)_6$); 2.35 (*s*, Me); 2.67 (*t*, ^3J = 8.1, CH_2); 4.44 (*q*, ^3J = 7.2, CH_2); 7.06 (*s*, H–C(5)); 10.68 (*s*, OH). ^{13}C-NMR (75 MHz): 13.6, 14.1, 20.0 (Me); 22.7, 26.7, 28.5, 29.2, 30.0, 31.9 (CH_2); 62.4 (CH_2O); 108.3 (C(1)); 119.6 (*t*, *J*(C,F) = 8.3, C(5)); 125.4 (*t*, *J*(C,F) = 288.0, CF_2Cl); 132.7 (*t*, *J*(C,F) = 26.1, C(6)); 133.9; 142.0; 159.2 (C); 170.0 (COO). ^{19}F-NMR (282 MHz): −43.8 (CF_2Cl). GC/MS (EI, 70 eV): 363 (M^+, 5), 362 (22), 303 (34), 302 (17), 301 (100), 299 (11), 280 (15), 279 (10), 234 (12), 233 (12), 232 (37), 214 (17), 212 (50), 196 (19). Anal. calc. for $C_{18}H_{25}ClF_2O_3$ (362.84): C 59.58, H 6.94; found: C 59.71, H 6.69.

Methyl 6-[Chloro(difluoro)methyl]-2-hydroxy-4-methyl-3-octylbenzoate (**3p**). Compound **1** (0.242 g, 1.0 mmol), *1-methoxy-1,3-bis(trimethylsilyloxy)dodeca-1,3-diene* (**2p**; 0.745 g, 2.0 mmol), and $TiCl_4$ (0.1 ml, 1.0 mmol) in CH_2Cl_2 (5 ml) gave **3p** (0.200 g, 55%). Colorless liquid. R_f (hexane/CH_2Cl_2 3:2) 0.60. IR (ATR): 2951*w*, 2920*m*, 2869*w*, 2850*m*, 1663*s*, 1608*w*, 1576*w*, 1472*w*, 1461*w*, 1438*m*, 1338*s*, 1294*s*, 1278*s*, 1099*s*, 975*s*, 960*s*, 805*s*. ^{1}H-NMR (300 MHz): 0.88 (*t*, ^3J = 6.7, Me); 1.28–1.52 (*m*, 12 H, $Me(CH_2)_6$); 2.35 (*s*, Me); 2.67 (*t*, ^3J = 7.7, ArCH_2); 3.95 (*s*, MeO); 7.06 (*s*, H–C(5)); 10.54 (*s*, OH). ^{13}C-NMR (75 MHz): 14.1, 20.0 (Me); 22.7, 26.7, 28.4, 29.3, 29.5, 30.0, 31.9 (CH_2); 52.4 (MeO); 108.0 (*t*, *J*(C,F) = 1.9, C(1)); 119.6 (*t*, *J*(C,F) = 8.7, C(5)); 125.4 (*t*, *J*(C,F) = 289.6, CF_2Cl); 132.7 (*t*, *J*(C,F) = 25.8, C(6)); 133.9; 142.2; 159.1 (C); 170.3 (COO). ^{19}F-NMR (282 MHz): −44.3 (CF_2Cl). GC/MS (EI, 70 eV): 362 (M^+, 22), 317 (34), 316 (17), 315 (100), 294 (15), 234 (12), 233 (13), 232 (36), 231 (24), 214 (17), 212 (51), 196 (20), 193 (12). Anal. calc. for $C_{18}H_{25}ClF_2O_3$ (362.84): C 59.58, H 6.94; found: C 59.57, H 6.94.

Methyl 6-[Chloro(difluoro)methyl]-2-hydroxy-4-methyl-3-nonylbenzoate (**3q**). Compound **1** (0.242 g, 1.0 mmol), *1-methoxy-1,3-bis(trimethylsilyloxy)trideca-1,3-diene* (**2q**; 0.773 g, 2.0 mmol), and $TiCl_4$ (0.1 ml, 1.0 mmol) in CH_2Cl_2 (5 ml) yielded **3q** (0.221 g, 59%). White solid. M.p. 36–37°. R_f (hexane/CH_2Cl_2 3:2) 0.79. IR (ATR): 2950*w*, 2920*m*, 2868*w*, 2849*m*, 1663*s*, 1608*w*, 1577*w*, 1472*m*, 1461*m*, 1438*m*, 1338*s*, 1099*s*, 977*s*, 966*s*, 804*s*. ^{1}H-NMR (300 MHz): 0.88 (*t*, ^3J = 6.7, Me); 1.27–1.52 (*m*,

Me(CH_2)$_7$); 2.35 (*s*, Me); 2.67 (*t*, ^3J = 7.4, ArCH_2); 3.95 (*s*, MeO); 7.06 (*s*, H–C(5)); 10.54 (*s*, OH). ^{13}C-NMR (75 MHz): 14.1, 20.0 (Me); 22.7, 26.7, 28.4, 29.3, 29.5, 29.6, 30.0, 31.9 (CH_2); 52.4 (MeO); 108.0 (*t*, *J*(C,F) = 1.9, C(1)); 119.6 (*t*, *J*(C,F) = 8.9, C(5)); 125.4 (*t*, *J*(C,F) = 289.6, CF_2Cl); 132.7 (*t*, *J*(C,F) = 25.8, C(6)); 133.9; 142.2; 159.1 (C); 170.3 (COO). ^{19}F-NMR (282 MHz): −44.3 (CF_2Cl). GC/MS (EI, 70 eV): 376 (M^+, 22), 331 (34), 330 (18), 329 (100), 308 (14), 234 (12), 233 (12), 232 (37), 231 (23), 214 (17), 212 (49), 196 (19), 193 (11). Anal. calc. for $C_{19}H_{27}ClF_2O_3$ (376.87): C 60.55, H 7.22; found: C 60.50, H 7.18.

Ethyl 6-[Chloro(difluoro)methyl]-3-decyl-2-hydroxy-4-methylbenzoate (**3r**). Compound **1** (0.242 g, 1.0 mmol), *1-ethoxy-1,3-bis(trimethylsilyloxy)tetradeca-1,3-diene* (**2r**; 0.829 g, 2.0 mmol), and $TiCl_4$ (0.1 ml, 1.0 mmol) in CH_2Cl_2 (5 ml) provided **3r** (0.138 g, 34%). Colorless liquid. R_f (hexane/CH_2Cl_2 3:2) 0.61. IR (ATR): 2956*w*, 2924*m*, 2854*m*, 1666*m*, 1607*w*, 1465*w*, 1392*m*, 1373*m*, 1271*s*, 1148*s*, 1112*s*, 990*s*, 802*s*, 721*m*. ^{1}H-NMR (300 MHz): 0.88 (*t*, ^3J = 6.7, Me); 1.26–1.53 (*m*, Me(CH_2)$_8$); 1.42 (*t*, ^3J = 7.1, Me); 2.34 (*s*, Me); 2.67 (*t*, ^3J = 7.7, ArCH_2); 4.43 (*q*, ^3J = 7.1, CH_2); 7.05 (*s*, H–C(5)); 10.67 (*s*, OH). ^{13}C-NMR (75 MHz): 13.6, 14.1, 20.0 (Me); 22.7, 26.6, 28.4, 29.3, 29.5, 29.6, 29.6, 30.0, 31.9 (CH_2); 62.3 (CH_2O); 108.2 (*t*, *J*(C,F) = 1.9, C(1)); 119.5 (*t*, *J*(C,F) = 8.7, C(5)); 125.4 (*t*, *J*(C,F) = 289.7, CF_2Cl); 132.6 (*t*, *J*(C,F) = 25.7, C(6)); 133.8; 142.0; 159.1 (C); 169.9 (COO). ^{19}F-NMR (282 MHz): −43.7 (CF_2Cl). GC/MS (EI, 70 eV): 404 (M^+, 18), 345 (33), 344 (20), 343 (100), 341 (10), 322 (14), 234 (12), 233 (11), 232 (37), 231 (21), 214 (17), 213 (10), 212 (47), 196 (18). Anal. calc. for $C_{21}H_{31}ClF_2O_3$ (404.92): C 62.29, H 7.72; found: C 62.30, H 7.62.

Methyl 6-[Chloro(difluoro)methyl]-3-dodecyl-2-hydroxy-4-methylbenzoate (**3s**). Compound **1** (0.242 g, 1.0 mmol), *1-methoxy-1,3-bis(trimethylsilyloxy)hexadeca-1,3-diene* (**2s**; 0.856 g, 2.0 mmol), and $TiCl_4$ (0.1 ml, 1.0 mmol) in CH_2Cl_2 (5 ml) gave **3s** (0.259 g, 62%). White solid. M.p. 52–53°. R_f (hexane/CH_2Cl_2 3:2) 0.70. IR (ATR): 2958*w*, 2915*m*, 2847*m*, 1663*m*, 1608*w*, 1472*m*, 1462*m*, 1438 *m*, 1338*s*, 1101*s*, 974*s*, 805*s*. ^{1}H-NMR (300 MHz): 0.88 (*t*, ^3J = 6.7, Me); 1.26–1.49 (*m*, Me(CH_2)$_{10}$); 2.35 (*s*, Me); 2.67 (*t*, ^3J = 7.8, ArCH_2); 3.95 (*s*, MeO); 7.06 (*s*, H–C(5)); 10.54 (*s*, OH). ^{13}C-NMR (75 MHz): 14.1 (Me); 20.0, 22.7, 26.6, 28.4, 29.3, 29.5, 29.6, 29.6, 29.7, 30.0, 31.9 (CH_2); 52.4 (MeO); 108.0 (*t*, *J*(C,F) = 1.9, C(1)); 119.6 (*t*, *J*(C,F) = 8.7, C(5)); 125.4 (*t*, *J*(C,F) = 289.6, CF_2Cl); 132.7 (*t*, *J*(C,F) = 25.7, C(6)); 133.9, 142.2, 159.1 (C), 170.3 (COO). ^{19}F-NMR (282 MHz): −44.3 (CF_2Cl). GC/MS (EI, 70 eV): 418 (M^+, 19), 373 (35), 372 (24), 371 (100), 350 (10), 234 (14), 233 (14), 232 (35), 231 (25), 214 (19), 212 (50), 196 (17), 193 (12), 43 (10). Anal. calc. for $C_{22}H_{33}ClF_2O_3$ (418.95): C 63.07, H 7.94; found: C 63.22, H 7.88.

Methyl 6-[Chloro(difluoro)methyl]-3-hexadecyl-2-hydroxy-4-methylbenzoate (**3t**). Compound **1** (0.242 g, 1.0 mmol), *1-methoxy-1,3-bis(trimethylsilyloxy)icosa-1,3-diene* (**2t**; 0.969 g, 2.0 mmol), and $TiCl_4$ (0.1 ml, 1.0 mmol) in CH_2Cl_2 (5 ml) afforded **3t** (0.196 g, 41%). White solid. M.p. 67–68°. R_f (hexane/CH_2Cl_2 3:2) 0.66. IR (ATR): 2983*w*, 2959*w*, 2915*s*, 2847*s*, 1663*s*, 1608*w*, 1472*m*, 1462*m*, 1438*m*, 1338*s*, 1286*s*, 1101*s*, 974*s*, 805*s*. ^{1}H-NMR (300 MHz): 0.88 (*t*, ^3J = 6.7, Me); 1.25–1.51 (*m*, 28 H, Me(CH_2)$_{14}$); 2.35 (*s*, Me); 2.67 (*t*, ^3J = 7.7, ArCH_2); 3.95 (*s*, MeO); 7.06 (*s*, H–C(5)); 10.54 (*s*, OH). ^{13}C-NMR (100 MHz): 14.1; 20.0 (Me); 22.7, 26.6, 28.4, 29.3, 29.5, 29.6, 29.7, 29.7, 30.0, 31.9 (CH_2); 52.4 (MeO); 108.0 (C(1)); 119.6 (*t*, *J*(C,F) = 8.7, C(5)); 125.4 (*t*, *J*(C,F) = 289.6, CF_2Cl); 132.7 (*t*, *J*(C,F) = 25.7, C(6)); 133.9; 142.1; 159.1 (C); 170.3 (COO). ^{19}F-NMR (282 MHz): −44.3 (CF_2Cl). GC/MS (EI, 70 eV): 475 (M^+, 6), 474 (26), 442 (14), 429 (30), 428 (22), 427 (100), 234 (15), 233 (13), 232 (54), 231 (21), 214 (16), 212 (57), 196 (15), 147 (13), 69 (12), 57 (15), 55 (14), 44 (12), 43 (15), 41 (12). Anal. calc. for $C_{26}H_{41}ClF_2O_3$ (475.05): C 65.74, H 8.70; found: C 65.58, H 8.69.

Methyl 6-[Chloro(difluoro)methyl]-2-hydroxy-4-methyl-3-(2-phenylethyl)benzoate (**3u**). Compound **1** (0.242 g, 1.0 mmol), *1-methoxy-1,3-bis(trimethylsilyloxy)-6-phenylhexa-1,3-diene* (**2u**; 0.729 g, 2.0 mmol), and $TiCl_4$ (0.1 ml, 1.0 mmol) in CH_2Cl_2 (5 ml) yielded **3u** (0.215 g, 61%). White solid. M.p. 56–57°. R_f (hexane/CH_2Cl_2 3:2) 0.56. IR (ATR): 3431*m*, 3086*w*, 3065*w*, 3030*w*, 2987*w*, 2952*w*, 2871*w*, 1689*s*, 1603*m*, 1570*w*, 1495*w*, 1452*m*, 1312*s*, 1106*s*, 1006*s*, 970*s*, 805*s*, 743*s*, 704*s*. ^{1}H-NMR (300 MHz): 2.22 (*s*, Me); 2.81 (*t*, ^3J = 4.6, CH_2); 2.96 (*t*, ^3J = 4.6, CH_2); 3.97 (*s*, MeO); 7.05 (*s*, H–C(5)); 7.17–7.35 (*m*, 5 arom. H); 10.68 (*s*, OH). ^{13}C-NMR (75 MHz): 19.9 (Me); 29.1; 34.4 (CH_2); 52.4 (MeO); 108.1 (*t*, *J*(C,F) = 1.9, C(1)); 119.6 (*t*, *J*(C,F) = 8.8, C(5)); 125.3 (*t*, *J*(C,F) = 289.7, CF_2Cl); 126.0, 128.4, 128.4, 132.6 (Ph); 133.1 (*t*, *J*(C,F) = 25.8, C(6)); 141.8, 142.5, 159.3 (C); 170.3 (COO). ^{19}F-NMR (282 MHz): −44.4 (CF_2Cl). GC/MS (EI, 70 eV): 354 (M^+, 26), 322 (15), 286 (13), 263 (21), 233 (34), 232 (11), 231 (100), 193 (10), 91 (39). Anal. calc. for $C_{18}H_{17}ClF_2O_3$ (354.78): C 60.94, H 4.83; found: C 60.88, H 4.77.

Methyl 6-[Chloro(difluoro)methyl]-3-[(4-fluorophenyl)methyl]-2-hydroxy-4-methylbenzoate (**3v**). Compound **1** (0.242 g, 1.0 mmol), *4-(4-fluorophenyl)-1-methoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene* (**2v**; 0.737 g, 2.0 mmol), and $TiCl_4$ (0.1 ml, 1.0 mmol) in CH_2Cl_2 (5 ml) gave **3v** (0.232 g, 65%). Colorless oil. R_f (hexane/CH_2Cl_2 3:2) 0.68. IR (ATR): 3040*w*, 3004*w*, 2955*w*, 2901*w*, 2855*w*, 1672*m*, 1604*m*, 1508*m*, 1438*m*, 1392*m*, 1274*s*, 1144*s*, 970*s*, 839*s*, 804*s*. ^{1}H-NMR (300 MHz): 2.32 (*s*, Me); 3.97 (*s*, MeO); 4.06 (*s*, ArCH_2); 6.92 (*s*, H–C(5)); 7.04–7.28 (*m*, 4 arom. H); 10.71 (*s*, OH). ^{13}C-NMR (100 MHz): 21.4 (Me); 32.1 (ArCH_2); 53.6 (MeO); 109.6 (C(1)); 116.1 (Ar); 120.8 (*t*, *J*(C,F) = 8.7, C(5)); 126.3 (*t*, *J*(C,F) = 289.8, CF_2Cl); 130.6 (Ar); 134.9 (*t*, *J*(C,F) = 26.0, C(6)); 132.4; 135.6; 144.4 (C); 160.3 (Ar); 161.2 (C); 171.2 (COO). ^{19}F-NMR (282 MHz): −44.6 (CF_2Cl), −44.7 (ArF). GC/MS (EI, 70 eV): 358 (M^+, 18), 338 (12), 327 (18), 323 (21), 322 (36), 318 (14), 308 (13), 307 (14), 306 (42), 305 (24), 303 (32), 302 (33), 291 (18), 290 (100), 289 (34), 288 (19), 287 (95), 219 (13), 215 (14), 214 (17), 212 (12), 183 (28). Anal. calc. for $C_{17}H_{14}ClF_3O_3$ (358.74): C 56.92, H 3.93; found: C 56.93, H 4.12.

Methyl 3-Chloro-6-[chloro(difluoro)methyl]-2-hydroxy-4-methylbenzoate (**3w**). Compound **1** (0.242 g, 1.0 mmol), *4-chloro-1-methoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene* (**2w**; 0.589 g, 2.0 mmol), and $TiCl_4$ (0.1 ml, 1.0 mmol) in CH_2Cl_2 (5 ml) yielded **3w** (0.101 g, 35%). Slightly yellow solid. M.p. 86–87°. R_f (heptane/AcOEt 3:2) 0.55. IR (ATR): 3377 *m*, 3047*w*, 2995*w*, 2961*w*, 2925*w*, 2850*w*, 1717*s*, 1601*m*, 1566*m*, 1455*m*, 1434*m*, 1409*m*, 1280*s*, 1121 *s*, 1112*s*, 974*s*, 950*s*, 853*s*, 807*s*. ^{1}H-NMR (300 MHz): 2.46 (*s*, Me); 3.99 (*s*, MeO); 7.17 (*s*, CH); 10.17 (*s*, OH). ^{13}C-NMR (75 MHz): 20.8 (Me); 52.9 (MeO); 110.7 (*t*, *J*(C,F) = 1.9, C(1)); 119.4 (*t*, *J*(C,F) = 8.5, C(5)); 124.7 (*t*, *J*(C,F) = 288.3, CF_2Cl); 125.9 (C(3)); 133.3 (*t*, *J*(C,F) = 26.2, C(6)); 142.0; 155.6 (C); 168.8 (O–CO). ^{19}F-NMR (282 MHz): −45.5 (CF_2Cl). GC/MS (EI, 70 eV): 285 (M^+, 3), 284 (28), 256 (12), 255 (16), 254 (67), 253 (26), 252 (199), 29 (16), 217 (25), 214 (11), 191 (13), 189 (41). Anal. calc. for $C_{10}H_8Cl_2F_2O_3$ (285.07): C 42.13, H 2.83; found: C 42.23, H 3.04.

Methyl 6-[Chloro(difluoro)methyl]-3-(3-chloropropyl)-2-hydroxy-4-methylbenzoate (**3x**). Compound **1** (0.242 g, 1.0 mmol), *7-chloro-1-methoxy-1,3-bis(trimethylsilyloxy)hepta-1,3-diene* (**2x**; 0.674 g, 2.0 mmol), and $TiCl_4$ (0.1 ml, 1.0 mmol) in CH_2Cl_2 (5 ml) furnished **3x** (0.205 g, 66%). Slightly yellow oil. R_f (hexane/CH_2Cl_2 3:2) 0.72. IR (ATR): 2955*w*, 2862*w*, 1671*m*, 1608*w*, 1573*w*, 1438*m*, 1392*w*, 1331*m*, 1280*s*, 1143*s*, 1109*m*, 973*s*, 802*s*. ^{1}H-NMR (300 MHz): 1.95–2.05 (*m*, CH_2); 2.39 (*s*, Me); 2.85 (*t*, ^3J = 7.7, ArCH_2); 3.60 (*t*, ^3J = 6.5, CH_2Cl); 3.96 (*s*, MeO); 7.09 (*s*, H–C(5)); 10.65 (*s*, OH). ^{13}C-NMR (75 MHz): 20.1 (Me); 24.1; 31.2; 45.0 (CH_2); 52.5 (MeO); 108.1 (*t*, *J*(C,F) = 1.9, C(1)); 119.7 (*t*, *J*(C,F) = 8.8, C(5)); 125.2 (*t*, *J*(C,F) = 289.7, CF_2Cl); 131.8 (C(3)); 133.3 (*t*, *J*(C,F) = 25.7, C(6)); 142.6; 159.2 (C); 170.2 (COO). ^{19}F-NMR (282 MHz): −44.6 (CF_2Cl). GC/MS (EI, 70 eV): 326 (M^+, 11), 290 (14), 261 (33), 260 (12), 259 (100), 255 (16), 212 (13). HR-MS (EI, 70 eV): 326.028160 ($C_{13}H_{14}Cl_2F_2O_3$; calc. 326.02826).

Methyl 6-[Chloro(difluoro)methyl]-3-(4-chlorobutyl)-2-hydroxy-4-methylbenzoate (**3y**). Compound **1** (0.242 g, 1.0 mmol), *8-chloro-1-methoxy-1,3-bis(trimethylsilyloxy)octa-1,3-diene* (**2y**; 0.413 g, 2.0 mmol), and $TiCl_4$ (0.1 ml, 1.0 mmol) in CH_2Cl_2 (5.0 ml) gave **3y** (0.212 g, 62%). Colorless oil. R_f (hexane/CH_2Cl_2 3:2) 0.57. IR (ATR): 3000*w*, 2955*w*, 2869*w*, 1671*s*, 1607*w*, 1438*m*, 1274*s*, 1143*s*, 1109*m*, 976*s*, 862 *m*, 802*m*, 739*w*. ^{1}H-NMR (300 MHz): 1.64–1.72 (*m*, CH_2); 1.83–1.92 (*m*, CH_2); 2.37 (*s*, Me); 2.72 (*t*, ^3J = 7.8, CH_2); 2.58 (*t*, ^3J = 6.6, CH_2); 3.96 (*s*, MeO); 7.08 (*s*, H–C(5)); 10.61 (*s*, OH). ^{13}C-NMR (75 MHz): 20.0 (Me); 25.6 (Me); 25.7 (CH_2); 32.5 (CH_2); 44.8 (CH_2); 52.5 (MeO); 108.15 (C(1)); 119.7 (*t*, *J*(C,F) = 8.9, C(5)); 125.3 (*t*, *J*(C,F) = 287.8, CF_2Cl); 132.9 (*t*, *J*(C,F) = 25.4, C(6)); 132.9; 142.4; 159.1 (C); 170.3 (COO). ^{19}F-NMR (282 MHz): −44.5 (CF_2Cl). GC/MS (EI, 70 eV): 341 (M^+, 2), 340 (13), 293 (15), 275 (35), 274 (16), 273 (100), 231 (19). Anal. calc. for $C_{14}H_{16}Cl_2F_2O_3$ (341.18): C 49.29, H 4.73; found: C 49.31, H 5.01.

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