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Regioselective synthesis of 4-alkyl- and 4-aryl-6-(perfluoroalkyl)salicylic acid derivatives by formal [3+3] cyclocondensation of 1,3-bis(silyloxy)-1,3-butadienes with 3-silyloxy-1-(perfluoroalkyl)prop-2-en-1-ones

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ABSTRACT

4-Alkyl- and 4-aryl-6-(perfluoroalkyl)salicylic acid derivatives were regioselectively prepared by [3+3] cyclization of 1,3-bis(silyl enol ethers) with 3-silyloxy-1-(perfluoroalkyl)prop-2-en-1-ones.

1. Introduction

Perfluoroalkyl groups are of considerable importance in the field of medicinal chemistry as they are chemically and biologically inert and are, thus, not metabolized.[1–3] The electronic properties of perfluoroalkyl-substituted products differ greatly from the alkyl-substituted analogues. This fact plays an important role in drug–receptor interactions. In addition, the in vivo transport of perfluoroalkyl-substituted molecules is improved, due to their increased lipophilicity. Because of the high chemical and biological stabilities of perfluoroalkyl groups, undesirable metabolic transformations are often avoided. Noteworthy, perfluoroalkyl-substituted molecules have received considerable attention also in material sciences. For example, various perfluoroalkyl-substituted compounds show amphiphilic properties and represent promising liquid crystals.[4] Perfluoroalkyl-substituted compounds also play an important role in catalytic reactions in fluorous biphase systems.[5]

(Perfluoroalkyl)arenes have been prepared by reaction of iodoarenes with (perfluoroalkyl)cuprates.[6] However, these reactions may suffer from a number of side reactions; in addition, the starting materials—functionalized arenes—are often not readily available. Fluorinated products are available also based on a building block strategy. For example, Portella and co-workers reported the synthesis of fluorophenols by annulation reactions of 2,2-difluoro-1,5 diketones, which were prepared from acylsilanes, trifluoromethyltrimethylsilane and enones.[7] They also studied the synthesis of *ortho*-perfluoroalkyl phenones from hemifluorinated enones,[8] the use of perfluoroketene dithioacetals and perfluorodithiocarboxylic acid derivatives as versatile tools for organofluorine synthesis,[9] the synthesis of new trifluoromethylated furans, dihydrofurans and butenolides from γ-ketothioesters[10] and a new strategy for the synthesis of fluorinated compounds by reaction of carboxylic acid dianions with perfluoroketene dithioacetals.[11] Haufe and co-workers reported the synthesis of new polyfluoroalkyl-containing pyrones, pyridones and pyrido[1,2-*a*]benzazoles from fluorinated β-alkoxyenones[12] and synthetic applications of β-fluoro-alkylated enones as dienophiles in Diels–Alder reactions.[13] Hu and Guan developed a new approach to 4-trifluoromethylpyridines and *meta*-trifluoromethylphenols based on the reaction of active methylene compounds with α-fluoroalkyl ketones and esters.[14]

Chan and co-workers reported[15] an elegant approach to salicylates based on cyclization of 1,3-bis(silyloxy)-1,3-butadienes[16] with 3-(silyloxy)alk-2-en-1-ones.[17] Recently, we developed a convenient access to fluorinated trifluoromethyl-[18] and perfluoroalkyl-substituted arenes[19] by cyclocondensation of 1,3-bis(silyloxy)-1,3-butadienes with 3-ethoxy-2-en-1-ones. Herein, we report the synthesis of a variety of 4-alkyl- and 4-aryl-6-(perfluoroalkyl)salicylic acid derivatives by, to the best of our knowledge, the first [3+3] cyclocondensations of 1,3-bis(silyloxy)-1,3-butadienes with 3-silyloxy-1-(perfluoroalkyl)prop-2-en-1-ones. These transformations provide a convenient and regioselective approach to a variety of perfluoroalkyl-substituted arenes, which are not readily available by other methods.

2. Results and discussion

Dicarbonyl compounds **3a–h,j,k,i** were prepared by Claisen condensation of ketones **1a–d** with perfluoroalkyl-substituted

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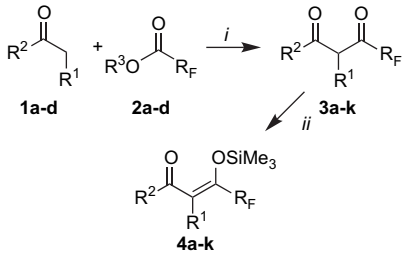


Scheme 1. Synthesis of **3a–w**: (i) NaOMe, $O(C_2H_5)_2$, 0→20 °C, 20 h; (ii) Me_3SiOTf (0.95 equiv), NEt_3 (1.0 equiv), Et_2O, 0 °C, 30 min, 20 °C, 3 days.

esters **2a–d** following a method reported by Moore and Levine.[20] The silylation of **3a–k**, following conditions reported by Krägeloh and Simchen,[21] afforded the novel 3-silyloxy-1-(perfluoroalkyl)prop-2-en-1-ones **4a–k** (Scheme 1, Table 1).

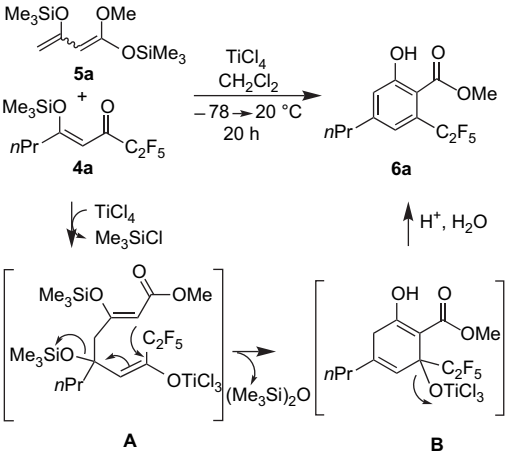
The $TiCl_4$ mediated cyclization of **4a–k** with 1,3-bis(silyl enol ethers) **5a–d**—prepared from methyl acetoacetate, pentane-2,4-dione, heptane-3,5-dione and methyl 3-oxohexanoate, respectively[15]—afforded the novel 5-alkyl- and 5-aryl-3-(perfluoroalkyl)phenols **6a–w** (Schemes 2 and 3, Table 2). All products were formed with very good regioselectivity. The formation of the products can be explained by $TiCl_4$ mediated 1,4-addition of the terminal carbon atom of the 1,3-bis(silyl enol ether) onto **4a–k** and subsequent cyclization by attack of the central carbon atom of the bis(silyl enol ether) onto the carbonyl group (Scheme 2).

Relatively good yields (50 and 65%) were obtained for products **6e** and **6k**, respectively, prepared from 1,3-bis(silyloxy)-1,3-butadiene **5d**. The latter is derived from methyl 3-oxohexanoate, i.e., a β-ketoester containing an ethyl group located at carbon atom C4. The yields of products **6a**,**d**,**g**,**j**,**n**,**p–r**,**v**, derived from the unsubstituted

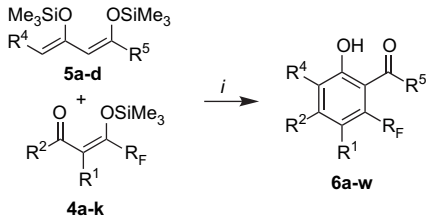
Table 1
Yields of **3a–k** and **4a–k**

1	2	3,4	R_F	R^1	R^2	R^3	**3**[a] (%)	**4**[a] (%)
a	**a**	**a**	C_2F_5	H	*n*-Pr	Et	59	92
b	**a**	**b**	C_2F_5	–$(CH_2)_3$–		Et	57	88
c	**a**	**c**	C_2F_5	H	Ph	Et	60	90
d	**b**	**d**	C_3F_7	H	Me	Et	47	82
a	**b**	**e**	C_3F_7	H	*n*-Pr	Et	80	80
b	**b**	**f**	C_3F_7	–$(CH_2)_3$–		Et	68	84
c	**b**	**g**	C_3F_7	H	Ph	Et	80	87
d	**c**	**h**	C_6F_{13}	H	Me	Me	70	92
a	**d**	**i**	C_7F_{15}	H	*n*-Pr	Me	70	94
b	**d**	**j**	C_7F_{15}	–$(CH_2)_3$–		Me	69	95
c	**d**	**k**	C_7F_{15}	H	Ph	Me	62	85

[a] Yields of isolated products.



Scheme 2. Possible mechanism for the formation of **6a**: (i) $TiCl_4$, CH_2Cl_2, −78→20 °C, 20 h.



Scheme 3. Synthesis of **6a–w**: (i) $TiCl_4$, CH_2Cl_2, −78→20 °C, 20 h.

Table 2
Yields of **6a–w**

4	5	6	R_F	R^1	R^2	R^4	R^5	**6**[a] (%)
a	**a**	**a**	C_2F_5	H	*n*-Pr	H	OMe	46
a	**b**	**b**	C_2F_5	H	*n*-Pr	H	Me	42
a	**c**	**c**	C_2F_5	H	*n*-Pr	Me	Et	33
b	**a**	**d**	C_2F_5	–$(CH_2)_3$–		H	OMe	57
b	**d**	**e**	C_2F_5	–$(CH_2)_3$–		Et	OMe	50
b	**b**	**f**	C_2F_5	–$(CH_2)_3$–		H	Me	40
c	**a**	**g**	C_2F_5	H	Ph	H	OMe	45
c	**b**	**h**	C_2F_5	H	Ph	H	Me	41
c	**c**	**i**	C_2F_5	H	Ph	Me	Et	37
d	**a**	**j**	C_3F_7	H	Me	H	OMe	45
d	**d**	**k**	C_3F_7	H	Me	Et	OMe	65
d	**b**	**l**	C_3F_7	H	Me	H	Me	40
d	**c**	**m**	C_3F_7	H	Me	Me	Et	37
e	**a**	**n**	C_3F_7	H	*n*-Pr	H	OMe	40
e	**c**	**o**	C_3F_7	H	*n*-Pr	Me	Et	31
f	**a**	**p**	C_3F_7	–$(CH_2)_3$–		H	OMe	41
g	**a**	**q**	C_3F_7	H	Ph	H	OMe	47
h	**a**	**r**	C_6F_{13}	H	Me	H	OMe	42
h	**b**	**s**	C_6F_{13}	H	Me	H	Me	41
i	**c**	**t**	C_7F_{15}	H	*n*-Pr	Me	Et	41
j	**c**	**u**	C_7F_{15}	–$(CH_2)_3$–		Me	Et	30
k	**a**	**v**	C_7F_{15}	H	Ph	H	OMe	36
k	**c**	**w**	C_7F_{15}	H	Ph	Me	Et	49

[a] Yields of isolated products.

β-ketoester-derived diene **5a**, are in the range of 36–57%. The yields decrease with the chain length of the perfluoroalkyl group. The yields of 1,3-diketone derived products (**6b**,**c**,**f**,**h**,**i**,**l**,**m**,**o**,**s**,**t**,**u**,**w**) are in most cases lower than those derived from ketoesters. This can be explained by their lower reactivity. A systematic influence of substituents R^1 and R^2 on the yield could not be observed.

The structures of all products were established by spectroscopic methods. The structures of **6c**,**g**,**j**,**l**,**q** were independently confirmed by X-ray crystal structural analysis (Figs. 1–5).[22] For all products, the carbonyl group is twisted out of the plane of the benzene moiety. In contrast, the two benzene moieties of derivatives **6g** and **6q** are only slightly twisted out of plane. No intramolecular hydrogen bonds O–H···O were observed. For derivatives **6j**,**l**,**q**,

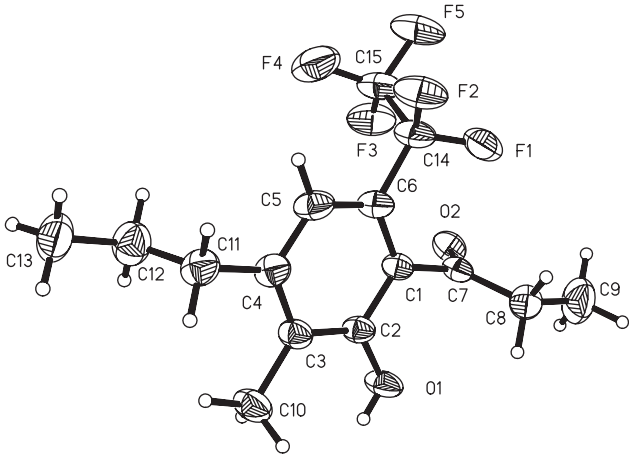


Figure 1. Ortep plot of **6c** (50% probability level).

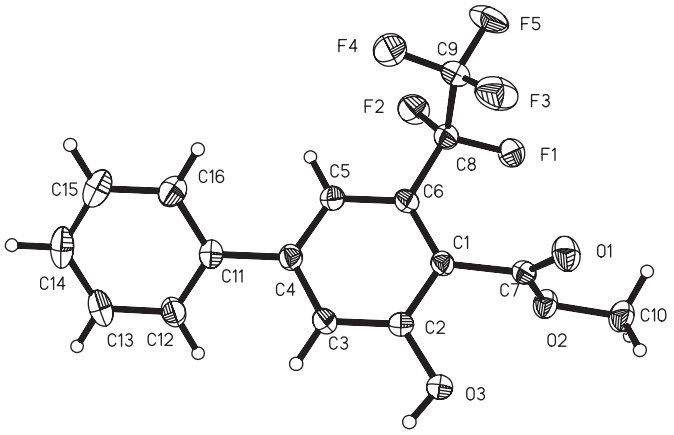


Figure 2. Ortep plot of **6g** (50% probability level).

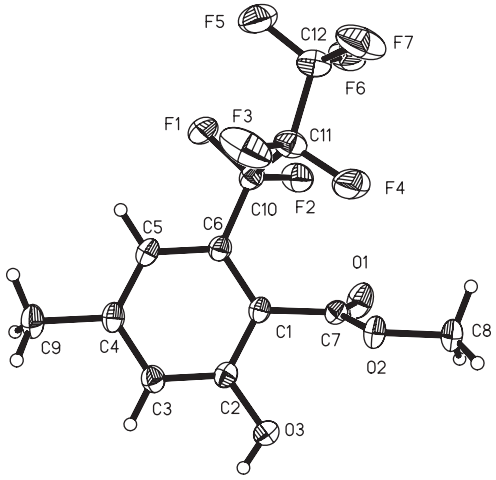


Figure 3. Ortep plot of **6j** (50% probability level).

containing a heptafluoropropyl group, an antiperiplanar conformation is observed for the RCF_2–CF_2R' moiety, due to steric reasons. Only a very small alternation of the bond lengths within the benzene moiety is observed.

3. Conclusions

In conclusion, a variety of novel 5-alkyl- and 5-aryl-3-(perfluoroalkyl)phenols were prepared by [3+3] cyclization of 1,3-bis(silyl enol ethers) with 3-silyloxy-1-(perfluoroalkyl)prop-2-en-1-ones.

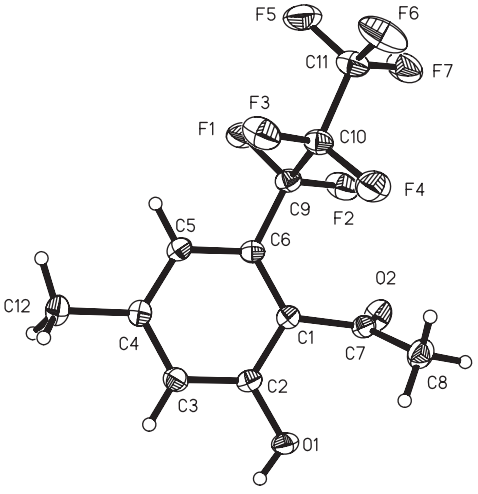


Figure 4. Ortep plot of **6l** (50% probability level).

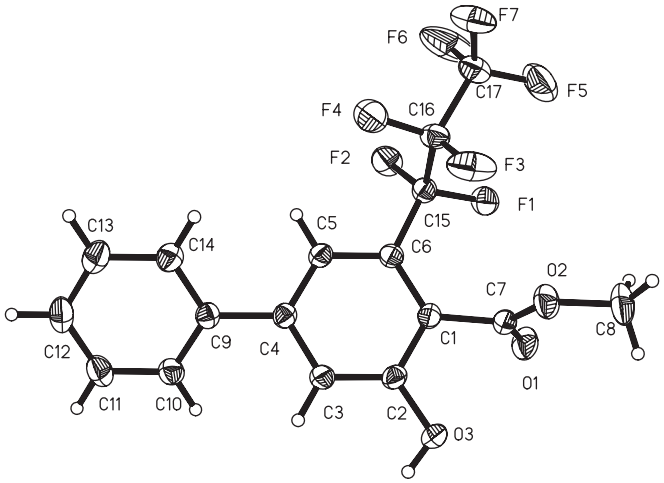


Figure 5. Ortep plot of **6q** (50% probability level).

4. Experimental section

4.1. General comments

All solvents were dried by standard methods and all reactions were carried out under an inert atmosphere. For ^1H and ^{13}C NMR spectra, the deuterated solvents indicated were used. Tetramethylsilane was used as the external standard. For ^{19}F NMR spectroscopy, $CFCl_3$ was used as the external standard. Mass spectrometric data (MS) were obtained by electron ionization (EI, 70 eV), chemical ionization (CI, H_2O) or electrospray ionization (ESI). For preparative scale chromatography, silica gel (60–200 mesh) was used. Melting points are uncorrected.

4.2. General procedure for the synthesis of perfluoroalkyldiones 3a–k

To a stirred solution of methanol (1.3 equiv) in diethyl ether (1 mL/1.0 mmol **1**) was added sodium (1.1 equiv) at 0 °C and stirring was continued for 30 min. Perfluorinated acid ester **2** (1.0 equiv) was added, the reaction mixture was stirred for 30 min and carbonyl compound **1** (1.0 equiv) was added. Then stirring was continued for 16 h at 20 °C. After addition of sulfuric acid (10%, 0.35 mL/mmol), the reaction mixture was extracted with diethyl ether. The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated under reduced pressure. The residue was purified by distillation.

*4.2.1. 1,1,1,2,2-Pentafluoro-octane-3,5-dione (**3a**)*

Starting with 2-pentanone **1a** (2.524 g, 30 mmol) and 2,2,3,3,3-pentafluoro-propionic acid ethyl ester **2a** (5.763 g, 30 mmol), **3a** was isolated as a colourless liquid (4.127 g, 59%), bp=70 °C/30 mbar (lit.[20a] 65.5 °C/30 mbar). ^1H NMR (250 MHz, $CDCl_3$): δ=0.99 (t, ^3J=7.4 Hz, 3H, $CH_2CH_2CH_3$), 1.62–1.78 (m, 2H, $CH_2CH_2CH_3$), 2.42 (t, ^3J=7.5 Hz, 2H, $CH_2CH_2CH_3$), 5.98 (s, 1H, CH); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−124.2 (m, CF_2), −82.8 (t, CF_3).

*4.2.2. 2-(2,2,3,3,3-Pentafluoro-propionyl)-cyclopentanone (**3b**)*

Starting with cyclopentanone **1b** (2.584 g, 30 mmol) and 2,2,3,3,3-pentafluoro-propionic acid ethyl ester **2a** (5.763 g, 30 mmol), **3b** was isolated as a colourless liquid (3.907 g, 57%), bp=72 °C/15 mbar (lit.[20a] 82 °C/30 mbar). ^1H NMR (250 MHz, $CDCl_3$): δ=2.00 (t, ^3J=7.6 Hz, 2H, $CH_2CH_2CH_2$), 2.52 (t, ^3J=7.9 Hz, 2H,

$CH_2CH_2CH_2$), 2.74–2.84 (m, 2H, $CH_2CH_2CH_2$), 13.46 (s, 1H, OH); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−121.9 (m, CF_2), −83.3 (t, CF_3).

*4.2.3. 4,4,5,5,5-Pentafluoro-1-phenyl-pentane-1,3-dione (**3c**)*

Starting with 1-phenyl-ethanone **1c** (1.056 g, 8.79 mmol) and 2,2,3,3,3-pentafluoro-propionic acid ethyl ester **2a** (1.689 g, 8.79 mmol), **3c** was isolated as a colourless liquid (1.002 g, 43%), bp=85 °C/4 mbar (lit.[20b] 75.5–76.5 °C/4 mbar). ^1H NMR (250 MHz, $CDCl_3$): δ=6.65 (s, 1H, CH), 7.48–7.57 (m, 2H, PhH), 7.60–7.69 (m, 1H, PhH), 7.92–8.01 (m, 2H, PhH), 15.32 (s, 1H, OH); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−123.9 (m, CF_2), −82.6 (t, CF_3).

*4.2.4. 5,5,6,6,7,7,7-Heptafluoro-heptane-2,4-dione (**3d**)*

Starting with acetone **1d** (1.952 g, 25 mmol) and 2,2,3,3,4,4,4-heptafluoro-butyric acid ethyl ester **2b** (6.052 g, 25 mmol), **3d** was isolated as a colourless liquid (3.014 g, 47%), bp=48 °C/20 mbar (lit.[20c] 55.5–56.8 °C/38–39 mbar). ^1H NMR (250 MHz, $CDCl_3$): δ=2.23 (s, 3H, CH_3), 5.97 (s, 1H, CH); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−127.0 (m, CF_2), −122.1 (m, CF_2), −80.7 (t, CF_3).

*4.2.5. 1,1,1,2,2,3,3-Heptafluoro-nonane-4,6-dione (**3e**)*

Starting with 2-pentanone **1a** (2.153 g, 25 mmol) and 2,2,3,3,4,4,4-heptafluoro-butyric acid ethyl ester **2b** (6.052 g, 25 mmol), **3e** was isolated as a colourless liquid (5.626 g, 80%), bp=75 °C/15 mmHg. ^1H NMR (250 MHz, $CDCl_3$): δ=0.99 (t, ^3J=7.4 Hz, 3H, $CH_2CH_2CH_3$), 1.62–1.78 (m, 2H, $CH_2CH_2CH_3$), 2.42 (t, ^3J=7.5 Hz, 2H, $CH_2CH_2CH_3$), 5.96 (s, 1H, CH); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−127.0 (m, CF_2), −122.0 (m, CF_2), −80.7 (t, CF_3).

*4.2.6. 2-(2,2,3,3,4,4,4-Heptafluoro-butyryl)-cyclopentanone (**3f**)*

Starting with cyclopentanone **1b** (2.103 g, 25 mmol) and 2,2,3,3,4,4,4-heptafluoro-butyric acid ethyl ester **2b** (6.052 g, 25 mmol), **3f** was isolated as a colourless liquid (4.771 g, 68%), bp=135 °C/760 mbar (lit.[20f] 45 °C/30 mbar). ^1H NMR (250 MHz, $CDCl_3$): δ=2.00 (t, ^3J=7.6 Hz, 2H, $CH_2CH_2CH_2$), 2.52 (t, ^3J=7.9 Hz, 2H, $CH_2CH_2CH_2$), 2.74–2.84 (m, 2H, $CH_2CH_2CH_2$), 13.47 (s, 1H, OH); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−127.2 (m, CF_2), −119.5 (m, CF_2), −80.7 (t, CF_3).

*4.2.7. 4,4,5,5,6,6,6-Heptafluoro-1-phenyl-hexane-1,3-dione (**3g**)*

Starting with 1-phenyl-ethanone **1c** (1.056 g, 8.79 mmol) and 2,2,3,3,4,4,4-heptafluoro-butyric acid ethyl ester **2b** (6.052 g, 25 mmol), **3g** was isolated as a colourless liquid (6.344 g, 80%), bp=65 °C/1 mbar (lit.[20g] 70 °C/0.1 mbar). ^1H NMR (250 MHz, $CDCl_3$): δ=6.63 (s, 1H, CH), 7.48–7.56 (m, 2H, PhH), 7.60–7.68 (m, 1H, PhH), 7.93–8.00 (m, 2H, PhH), 15.32 (s, 1H, OH); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−126.8 (m, CF_2), −121.7 (m, CF_2), −80.6 (t, CF_3).

*4.2.8. 5,5,6,6,7,7,8,8,9,9,10,10,10-Tridecafluoro-decane-2,4-dione (**3h**)*

Starting with acetone **1d** (1.405 g, 18 mmol) and 2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoro-heptanoic acid methyl ester **2c** (6.806 g, 18 mmol), **3h** was isolated as a colourless liquid (5.122 g, 70%), bp=95 °C/15 mbar. ^1H NMR (250 MHz, $CDCl_3$): δ=2.23 (s, 3H, CH_3), 5.97 (s, 1H, CH); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−126.2 (m, CF_2), −122.9 (m, CF_2), −122.6 (m, CF_2), −121.8 (m, CF_2), −121.1 (m, CF_2), −80.9 (t, CF_3).

*4.2.9. 7,7,8,8,9,9,10,10,11,11,12,12,13,13,13-Pentadecafluoro-tridecane-4,6-dione (**3i**)*

Starting with 2-pentanone **1a** (1.034 g, 12 mmol) and 2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-pentadecafluoro-octanoic acid methyl ester **2d** (5.137 g, 12 mmol), **3i** was isolated as a colourless liquid (4.040 g, 70%), bp=110 °C/3 mbar. ^1H NMR (250 MHz, $CDCl_3$): δ=0.99 (t, ^3J=7.4 Hz, 3H, $CH_2CH_2CH_3$), 1.62–1.79 (m, 2H, $CH_2CH_2CH_3$), 2.42 (t, ^3J=7.5 Hz, 2H, $CH_2CH_2CH_3$), 5.96 (s, 1H, CH), 14.60 (s, 1H, OH); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−126.1 (m, CF_2), −122.8 (m, CF_2), −122.5 (m, CF_2), −122.0 (m, CF_2), −121.6 (m, CF_2), −121.0 (m, CF_2), −80.8 (t, CF_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=13.5 (CH_3), 19.0 (CH_2), 40.0 (CH_2), 97.2 (CH), 178.0 (t, ^2J=26.4 Hz, $COCH_2$), 196.4 (CF_2COH). MS (EI, 70 eV): *m*/*z* (%)=482 (M^+, 5), 454 (13), 439 (67), 113 (100); HRMS (ESI, 70 eV) calcd for $C_{13}H_9F_{15}O_2$ ($[M+H]^+$): 483.04358, found: 483.04328. Anal. Calcd for $C_{13}H_9F_{15}O_2$ (482.19): C, 32.38; H, 1.88. Found: C, 32.24; H, 1.73.

*4.2.10. 2-(2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-Pentadecafluoro-octanoyl)-cyclopentanone (**3j**)*

Starting with cyclopentanone **1b** (2.103 g, 25 mmol) and 2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-pentadecafluoro-octanoic acid methyl ester **2d** (5.137 g, 12 mmol), **3j** was isolated as a colourless liquid (3.979 g, 69%), bp=72 °C/0.5 mbar (lit.[20f] 75 °C/0.8 mbar). ^1H NMR (250 MHz, $CDCl_3$): δ=2.00 (t, ^3J=7.5 Hz, 2H, $CH_2CH_2CH_2$), 2.53 (t, ^3J=7.9 Hz, 2H, $CH_2CH_2CH_2$), 2.74–2.85 (m, 2H, $CH_2CH_2CH_2$), 13.51 (s, 1H, OH); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−126.1 (m, CF_2), −122.7 (m, 4F, CF_2), −122.0 (m, CF_2), −121.8 (m, CF_2), −118.5 (m, CF_2), −80.8 (t, CF_3).

*4.2.11. 4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Pentadecafluoro-1-phenyl-pentane-1,3-dione (**3k**)*

Starting with 1-phenyl-ethanone **1c** (1.081 g, 9.00 mmol) and 2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-pentadecafluoro-octanoic acid methyl ester **2d** (3.853 g, 9 mmol), **3k** was isolated as a colourless liquid (2.881 g, 62%), bp=115 °C/0.5 mbar. ^1H NMR (250 MHz, $CDCl_3$): δ=6.62 (s, 1H, CH), 7.47–7.57 (m, 2H, PhH), 7.60–7.68 (m, 1H, PhH), 7.93–8.01 (m, 2H, PhH), 15.30 (s, 1H, OH); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−126.1 (m, CF_2), −122.7 (m, CF_2), −122.3 (m, CF_2), −122.0 (m, CF_2), −121.5 (m, CF_2), −120.6 (m, CF_2), −80.8 (t, CF_3).

4.3. General procedure for the synthesis of 3-silyloxy-1-(perfluoroalkyl)prop-2-en-1-ones 4a–k

To a stirred solution of perfluoralkyl-dione **3** (1.0 equiv) in diethyl ether (2 mL/1.0 mmol **3**), triethylamine (1.0 equiv) and TMSOTf (0.95 equiv) were added at 0 °C under an argon atmosphere. The solution was stirred for 30 min at 0 °C. The temperature of the reaction mixture was allowed to rise to 20 °C and stirring was continued for 3 days. A liquid salt layer separated at the bottom of the flask. The upper layer (ether solution containing the product) was transferred to a dry flask by syringe under an argon atmosphere. Diethyl ether (1.5 mL/mmol **3**) was added to the liquid salt layer, the mixture was stirred for 2 min and the layers were allowed to separate within 2 h. The ether solutions were combined and concentrated in vacuo. Due to their unstable nature, silyl enol ethers **4a–k** were directly used for the synthesis of phenols **6a–w**.

4.4. General procedure for the synthesis of 3-(perfluoroalkyl)phenols 6a–w

To a stirred dichloromethane solution (2 mL/1.0 mmol of **4**) of silyl enol ether **4** (1.0 equiv) and of 1,3-bis(silyl enol ether) **5** (1.1 equiv) was added $TiCl_4$ (1.1 equiv) at −78 °C under an argon atmosphere. The temperature of the reaction mixture was allowed to rise to 20 °C in 16 h. To the solution was added hydrochloric acid (10%, 3 mL/mmol) and the mixture was extracted with dichloromethane (3×15 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, heptanes→EtOAc/heptanes=1:10).

*4.4.1. 2-Hydroxy-6-pentafluoroethyl-4-propyl-benzoic acid methyl ester (**6a**)*

Starting with silyl enol ether **4a** (0.620 g, 2.04 mmol), 1,3-bis-silyl enol ether **5a** (0.574 g, 2.20 mmol) and $TiCl_4$ (0.24 mL,

2.20 mmol), **6a** was isolated as a pale yellow solid (0.294 g, 46%), mp=43 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=0.95 (t, ^3J=7.3 Hz, 3H, CH_2CH_3), 1.57–1.74 (m, 2H, CH_2CH_3), 2.61 (t, ^3J=7.6 Hz, 2H, $ArCH_2$), 3.93 (s, 3H, OCH_3), 7.02 (s, 2H, Ar*H*), 9.48 (s, 1H, O*H*); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−103.0 (m, CF_2), −80.9 (t, CF_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=13.6 (CH_2CH_3), 23.7 (CH_2), 37.8 (CH_2), 52.7 (OCH_3), 111.5 (t, ^3J=2.2 Hz, CCO_2CH_3), 121.0 (*C*HCOH), 121.3 (t, ^3J=8.9 Hz, $CHCC_2F_5$), 128.7 (t, ^2J=23.0 Hz, CC_2F_5), 148.9 (CC_3H_7), 159.7 (*C*OH), 169.2 (*C*O); IR (ATR, cm^{-1}): ν=3286 (m), 2965 (w), 2940 (w), 2879 (w), 1708 (s), 1614 (m), 1585 (w), 1434 (m), 1307 (m), 1277 (m), 1208 (s), 1174 (m), 1154 (m), 1135 (m), 1090 (m), 1038 (s), 990 (m); MS (EI, 70 eV): *m*/*z* (%)=312 (M$^+$, 32), 280 (96), 252 (100), 223 (40); HRMS (EI, 70 eV) calcd for $C_{13}H_{13}F_5O_3$ (M$^+$): 312.07794, found: 312.07795. Anal. Calcd for $C_{13}H_{13}F_5O_3$ (312.23): C, 50.01; H, 4.20. Found: C, 50.17; H, 4.21.

4.4.2. 1-(2-Hydroxy-6-pentafluoroethyl-4-propyl-phenyl)-ethanone (**6b**)

Starting with silyl enol ether **4a** (0.573 g, 1.88 mmol), 1,3-bis-silyl enol ether **5b** (0.538 g, 2.20 mmol) and $TiCl_4$ (0.24 mL, 2.20 mmol), **6b** was isolated as a colourless solid (0.237 g, 42%), mp=108 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=0.92 (t, ^3J=7.3 Hz, 3H, CH_2CH_3), 1.51–1.69 (m, 2H, CH_2CH_3), 2.53 (t, ^3J=7.7 Hz, 2H, $ArCH_2$), 2.53 (s, 3H, $COCH_3$), 6.84 (s, 1H, Ar*H*), 6.91 (s, 1H, Ar*H*), 7.04 (s, 1H, O*H*); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−107.2 (m, CF_2), −83.5 (t, CF_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=13.5 (CH_2CH_3), 23.9 (CH_2), 32.2 ($COCH_3$), 37.5 (CH_2), 119.8 (t, ^3J=7.2 Hz, $CHCC_2F_5$), 119.9 (*C*HCOH), 125.2 (t, ^2J=23.4 Hz, CC_2F_5), 126.2 (t, ^3J=2.7 Hz, *C*COCH$_3$), 146.0 (CC_3H_7), 153.1 (*C*OH), 205.8 (*C*O); IR (ATR, cm^{-1}): ν=3244 (m), 2971 (w), 2941 (w), 2865 (w), 1687 (m), 1614 (m), 1585 (w), 1433 (m), 1357 (m), 1321 (m), 1281 (m), 1200 (s), 1173 (m), 1145 (m), 1134 (s), 1047 (m), 987 (m). MS (EI, 70 eV): *m*/*z* (%)=296 (M$^+$, 11), 281 (100), 233 (10); HRMS (EI, 70 eV) calcd for $C_{13}H_{13}F_5O_2$ (M$^+$): 296.08302, found: 296.08316.

4.4.3. 1-(2-Hydroxy-3-methyl-6-pentafluoroethyl-4-propyl-phenyl)-propan-1-one (**6c**)

Starting with silyl enol ether **4a** (0.619 g, 2.04 mmol), 1,3-bis-silyl enol ether **5c** (0.600 g, 2.20 mmol) and $TiCl_4$ (0.24 mL, 2.20 mmol), **6c** was isolated as a yellow solid (0.216 g, 33%), mp=72 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=0.97 (t, ^3J=7.3 Hz, 3H, $CH_2CH_2CH_3$), 1.17 (t, ^3J=7.2 Hz, 3H, $COCH_2CH_3$), 1.50–1.66 (m, 2H, $CH_2CH_2CH_3$), 2.21 (s, 3H, $ArCH_3$), 2.61 (t, ^3J=7.7 Hz, 2H, $ArCH_2$), 2.79 (q, ^3J=7.2 Hz, 2H, $COCH_2$), 6.11 (s, 1H, O*H*), 6.95 (s, 1H, Ar*H*); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−107.0 (m, CF_2), −83.4 (t, CF_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=7.9 (CH_3), 11.5 (CH_3), 13.8 (CH_3), 23.2 (CH_2), 35.8 (CH_2), 38.1 (CH_2), 120.8 (t, ^3J=7.3 Hz, $CHCC_2F_5$), 122.3 (t, ^2J=23.5 Hz, CC_2F_5), 125.9 (t, ^3J=2.7 Hz, $CCOCH_2CH_3$), 128.0 (*C*), 143.8 (*C*), 151.0 (*C*OH), 207.9 (*C*O); IR (ATR, cm^{-1}): ν=3435 (m), 2977 (w), 2958 (w), 2943 (w), 2874 (w), 1699 (m), 1609 (w), 1573 (w), 1310 (m), 1194 (s), 1172 (s), 1134 (m), 1109 (m), 1096 (m), 1054 (m), 1025 (m). MS (EI, 70 eV): *m*/*z* (%)=324 (M$^+$, 5), 295 (100), 247 (12), 69 (15); HRMS (EI, 70 eV) calcd for $C_{15}H_{17}F_5O_2$ (M$^+$): 324.11432, found: 324.11393. Anal. Calcd for $C_{15}H_{17}F_5O_2$ (324.29): C, 55.56; H, 5.28. Found: C, 55.63; H, 5.24.

Crystal data of **6c**. Empirical formula: $C_{15}H_{17}F_5O_2$. Formula weight: 324.29. Temperature: 173(2) K. Wavelength: 0.71073 Å. Crystal system: monoclinic. Space group (H.-M.): $P2_1/c$. Space group (Hall): $-P2ybc$. Unit cell dimensions: a=5.97150(10) Å, α=90°, b=22.7779(5) Å, β=99.6550(10)°, c=11.7411(3) Å, γ=90°. Volume: 1574.38(6) Å^3; Z=4. Density (calculated): 1.368 Mg/m^3. Absorption coefficient: 0.128 mm^{-1}. F(000)=672. Crystal size: 0.47×0.30×0.09 mm^3. Θ Range for data collection: 2.51–29.99°. Index ranges: $-8\leq h\leq 8$, $-28\leq k\leq 32$, $-16\leq l\leq 16$. Reflections collected: 21,080. Independent reflections: 4597 [R(int)=0.0342]. Completeness to Θ=29.99°: 99.9%. Absorption correction: semi-empirical from equivalents. Max. and min. transmissions: 0.9885 and 0.9421. Refinement method: full-matrix least-squares on F^2. Data/restraints/parameters: 4597/0/206. Goodness-of-fit on F^2: 1.028. Final R indices [$I>2\sigma(I)$]: $R1$=0.0501, $wR2$=0.1211. R indices (all data): $R1$=0.0869, $wR2$=0.1453. Largest diff. peak and hole: 0.512 and −0.257 e/Å^3.

4.4.4. 6-Hydroxy-4-pentafluoroethyl-indane-5-carboxylic acid methyl ester (**6d**)

Starting with silyl enol ether **4b** (0.607 g, 2.01 mmol), 1,3-bis-silyl enol ether **5a** (0.574 g, 2.20 mmol) and $TiCl_4$ (0.24 mL, 2.20 mmol), **6d** was isolated as a pale yellow solid (0.354 g, 57%), mp=137 °C; ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.97–2.11 (m, 2H, $ArCH_2CH_2$), 2.88 (t, ^3J=7.5 Hz, 2H, $ArCH_2$), 3.00 (t, ^3J=7.3 Hz, 2H, $ArCH_2$), 3.90 (s, 3H, CH_3), 7.02 (s, 1H, Ar*H*), 8.20 (s, 1H, O*H*); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−102.1 (m, CF_2), −79.1 (t, CF_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=25.4 (CH_2), 32.7 (CH_2), 32.9 (CH_2), 52.7 (CH_3), 114.2 (t, ^3J=3.9 Hz, CCC_2F_5), 116.8 (*C*HCOH), 124.2 (t, ^2J=23.5 Hz, CC_2F_5), 137.0 (t, ^3J=4.1 Hz, CCC_2F_5), 151.6 (*C*CHCOH), 156.5 (*C*OH), 169.5 (*C*O); IR (ATR, cm^{-1}): ν=3329 (m), 3004 (w), 2962 (w), 2853 (w), 1698 (m), 1606 (w), 1447 (m), 1437 (m), 1289 (m), 1191 (m), 1181 (m), 1165 (m), 1133 (m), 1117 (m), 1027 (m). MS (EI, 70 eV): *m*/*z* (%)=310 (M$^+$, 13), 278 (100), 149 (32), 131 (15); HRMS (EI, 70 eV) calcd for $C_{13}H_{11}F_5O_3$ (M$^+$): 310.06229, found: 310.06187. Anal. Calcd for $C_{13}H_{11}F_5O_3$ (310.22): C, 50.33; H, 3.57. Found: C, 50.48; H, 3.38.

4.4.5. 7-Ethyl-6-hydroxy-4-pentafluoroethyl-indan-5-carboxylic acid methyl ester (**6e**)

Starting with silyl enol ether **4b** (0.456 g, 1.51 mmol), 1,3-bis-silyl enol ether **5d** (0.480 g, 1.66 mmol) and $TiCl_4$ (0.18 mL, 1.65 mmol), **6e** was isolated as a yellow solid (0.234 g, 50%), mp=65 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.15 (t, ^3J=7.5 Hz, 3H, CH_2CH_3), 1.97–2.11 (m, 2H, $ArCH_2CH_2$), 2.66 (q, ^3J=7.5 Hz, 2H, CH_2CH_3), 2.88 (t, ^3J=7.5 Hz, 2H, $ArCH_2$), 3.02 (t, ^3J=7.4 Hz, 2H, $ArCH_2$), 3.90 (s, 3H, CH_3), 8.48 (s, 1H, O*H*); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−101.0 (m, CF_2), −78.8 (t, CF_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=12.8 (CH_2CH_3), 21.1 (CH_2), 24.9 (CH_2), 31.2 (CH_2), 33.1 (CH_2), 52.6 (CH_3), 113.4 (t, ^3J=3.9 Hz, CCC_2F_5), 121.5 (t, ^2J=23.4 Hz, CC_2F_5), 132.2 (CCH_2CH_3), 136.5 (t, ^3J=4.1 Hz, CCC_2F_5), 149.7 ($CCCH_2CH_3$), 154.6 (*C*OH), 170.3 (*C*O); IR (ATR, cm^{-1}): ν=3235 (w), 3012 (w), 2963 (w), 2935 (w), 2874 (w), 1673 (m), 1593 (w), 1463 (w), 1444 (m), 1340 (m), 1292 (m), 1195 (s), 1162 (s), 1119 (m), 1096 (m), 1070 (m), 1050 (m), 1038 (m), 997 (m); MS (EI, 70 eV): *m*/*z* (%)=338 (M$^+$, 23), 306 (100), 278 (27); HRMS (EI, 70 eV) calcd for $C_{15}H_{15}F_5O_3$ (M$^+$): 338.09359, found 338.09297.

4.4.6. 1-(6-Hydroxy-4-pentafluoroethyl-indan-5-yl)-ethanone (**6f**)

Starting with silyl enol ether **4b** (0.611 g, 2.02 mmol), 1,3-bis-silyl enol ether **5b** (0.538 g, 2.20 mmol) and $TiCl_4$ (0.24 mL, 2.20 mmol), **6f** was isolated as a colourless solid (0.240 g, 40%), mp=146 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.97–2.10 (m, 2H, $ArCH_2CH_2$), 2.51 (s, 3H, CH_3), 2.80 (t, ^3J=7.5 Hz, 2H, $ArCH_2$), 2.97 (t, ^3J=7.3 Hz, 2H, $ArCH_2$), 6.24 (s, 1H, O*H*), 6.83 (s, 1H, Ar*H*); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−107.2 (m, CF_2), −83.0 (t, CF_3); ^{13}C NMR (63 MHz, $CDCl_3$): δ=25.4 (CH_2), 32.1 (CH_2), 32.3 (CH_3), 32.5 (CH_2), 116.3 (*C*HCOH), 120.7 (t, ^2J=23.4 Hz, CC_2F_5), 128.0 (t, ^3J=3.9 Hz, CCC_2F_5), 136.1 (t, ^3J=4.1 Hz, CCC_2F_5), 148.5 (*C*CHCOH), 151.1 (*C*OH), 205.5 (*C*O); IR (ATR, cm^{-1}): ν=3254 (w), 2977 (w), 2946 (w), 2894 (w), 2850 (w), 1694 (m), 1605 (w), 1445 (w), 1433 (w), 1304 (m), 1230 (m), 1219 (m), 1198 (m), 1179 (m), 1160 (m), 1130 (m), 1047 (m), 1024 (m); MS (EI, 70 eV): *m*/*z* (%)=294 (M$^+$, 21), 279 (100), 231 (14), 133 (7); HRMS (EI, 70 eV) calcd for $C_{13}H_{11}F_5O_2$ (M$^+$): 294.06737, found 294.06718. Anal. Calcd for $C_{13}H_{11}F_5O_2$ (294.22): C, 53.07; H, 3.77. Found: C, 53.14; H, 3.64.

4.4.7. 3-Hydroxy-5-pentafluoroethyl-biphenyl-4-carboxylic acid methyl ester (**6g**)

Starting with silyl enol ether **4c** (0.677 g, 2.00 mmol), 1,3-bis-silyl enol ether **5a** (0.573 g, 2.20 mmol) and $TiCl_4$ (0.24 mL, 2.20 mmol), **6g** was isolated as a colourless solid (0.309 g, 45%), mp=142 °C. ^1H NMR (250 MHz, $CDCl_3$): δ=3.98 (s, 3H, OCH_3), 7.40–7.64 (m, 7H, Ar*H*), 9.55 (s, 1H, O*H*); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−103.1 (m, CF_2), −80.8 (t, CF_3); ^{13}C NMR (63 MHz, $CDCl_3$): δ=52.9 (OCH_3), 112.7 (*C*CO_2CH_3), 119.5 (*C*HCOH), 119.6 (t, ^3J=9.2 Hz, *C*HCC_2F_5), 127.2 (Ph), 129.0 (Ph), 129.1 (Ph), 129.5 (t, ^2J=23.2 Hz, *C*C_2F_5), 138.3 (*C*), 146.2 (*C*), 159.9 (*C*OH), 169.1 (*C*O); IR (ATR, cm^{-1}): ν=3389 (m), 3040 (w), 3010 (w), 2956 (w), 1722 (s), 1614 (m), 1573 (m), 1412 (m), 1299 (m), 1217 (s), 1193 (s), 1154 (s), 1042 (s); MS (EI, 70 eV): *m*/*z* (%)=346 (M^+, 41), 314 (100), 286 (24), 217 (34), 188 (15), 108 (14); HRMS (EI, 70 eV) calcd for $C_{16}H_{11}F_5O_3$ (M^+): 346.06229, found 346.06246. Anal. Calcd for $C_{16}H_{11}F_5O_3$ (346.25): C, 55.50; H, 3.20. Found: C, 55.72; H, 2.94.

Crystal data of **6g**. Empirical formula: $C_{16}H_{11}F_5O_3$. Formula weight: 346.25. Temperature: 173(2) K. Wavelength: 0.71073 Å. Crystal system: monoclinic. Space group (H.-M.): $P2_1/c$. Space group (Hall): −*P*2*ybc*. Unit cell dimensions: a=9.6140(3) Å, α=90°, b=15.1090(5) Å, β=91.042(2)°, c=10.3975(3) Å, γ=90°. Volume: 1510.07(8) $Å^3$; Z=4. Density (calculated) 1.523 Mg/m^3. Absorption coefficient: 0.145 mm^{-1}. F(000)=704 . Crystal size: 0.56×0.44×0.18 mm^3. Θ Range for data collection: 2.51–30.00°. Index ranges: $-13\le h\le 13$, $-18\le k\le 21$, $-14\le l\le 13$. Reflections collected: 19,091. Independent reflections: 4409 [R(int)=0.0225]. Completeness to Θ=30.00°: 99.9%. Absorption correction: semi-empirical from equivalents. Max. and min. transmissions: 0.9744 and 0.9234. Refinement method: full-matrix least-squares on F^2. Data/restraints/parameters 4409/0/223. Goodness-of-fit on F^2: 1.034. Final R indices [$I>2\sigma(I)$]: $R1$=0.0365, $wR2$=0.0973. R indices (all data): $R1$=0.0445, $wR2$=0.1057. Extinction coefficient: 0.0127(16). Largest diff. peak and hole: 0.397 and −0.275 e/$Å^3$.

4.4.8. 1-(3-Hydroxy-5-pentafluoroethyl-biphenyl-4-yl)-ethanone (**6h**)

Starting with silyl enol ether **4c** (0.626 g, 2.06 mmol), 1,3-bis-silyl enol ether **5b** (0.538 g, 2.20 mmol) and $TiCl_4$ (0.24 mL, 2.20 mmol), **6h** was isolated as a colourless solid (0.279 g, 41%), mp=141 °C. ^1H NMR (250 MHz, $CDCl_3$): δ=2.60 (s, 3H, CH_3), 6.76 (s, 1H, O*H*), 7.27 (s, 1H, Ar*H*), 7.34 (s, 1H, Ar*H*), 7.41–7.56 (m, 5H, Ph*H*); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−106.9 (m, CF_2), −83.2 (t, CF_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ=32.2 (*C*H_3), 118.5 (*C*HCOH), 118.7 (t, ^3J=6.5 Hz, *C*HCC_2F_5), 126.1 (t, ^2J=23.5 Hz, *C*C_2F_5), 127.0 (*C*), 127.2 (Ph), 128.6 (Ph), 129.0 (Ph), 138.5 (*C*), 144.1 (*C*), 153.5 (*C*OH), 204.8 (*C*O); IR (ATR, cm^{-1}): ν=3381 (w), 3066 (w), 3033 (w), 2927 (w), 1700 (m), 1612 (m), 1409 (m), 1319 (m), 1197 (s), 1142 (m), 1045 (m); MS (EI, 70 eV): *m*/*z* (%)=330 (M^+, 39), 315 (100), 267 (23); HRMS (EI, 70 eV) calcd for $C_{16}H_{11}F_5O_2$ (M^+): 330.06737, found 330.06706.

4.4.9. 1-(3-Hydroxy-2-methyl-5-pentafluoroethyl-biphenyl-4-yl)-propan-1-one (**6i**)

Starting with silyl enol ether **4c** (0.668 g, 1.97 mmol), 1,3-bis-silyl enol ether **5c** (0.600 g, 2.20 mmol) and $TiCl_4$ (0.24 mL, 2.20 mmol), **6i** was isolated as a yellow solid (0.262 g, 37%), mp=126 °C. ^1H NMR (250 MHz, $CDCl_3$): δ=1.22 (t, ^3J=7.3 Hz, 3H, CH_2CH_3), 2.21 (s, 3H, ArCH_3), 2.85 (q, ^3J=7.3 Hz, 2H, CH_2CH_3), 5.84 (s, 1H, O*H*), 7.09 (s, 1H, Ar*H*), 7.23–7.50 (m, 5H, Ph*H*); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−107.3 (m, CF_2), −83.4 (t, CF_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=7.8 (*C*H_3), 13.4 (*C*H_3), 38.1 (*C*H_2), 122.0 (t, ^3J=7.4 Hz, *C*HCC_7F_{15}), 122.8 (t, ^2J=23.9 Hz, *C*C_7F_{15}), 127.5 (*C*), 127.7 (*C*), 127.9 (Ph), 128.4 (Ph), 129.0 (Ph), 139.6 (*C*), 144.3 (*C*), 151.0 (*C*OH), 206.9 (*C*O); IR (ATR, cm^{-1}): ν=3412 (w), 3055 (w), 2986 (w), 2944 (w), 2906 (w), 2884 (w), 1704 (m), 1599 (w), 1564 (w), 1204 (s), 1142 (s), 1128 (s), 1099 (m); MS (EI, 70 eV): *m*/*z* (%)=358 (M^+, 10), 329 (100), 281 (18), 183 (7); HRMS (EI, 70 eV) calcd for $C_{18}H_{15}F_5O_2$ (M^+): 358.09867, found 358.09878. Anal. Calcd for $C_{18}H_{15}F_5O_2$ (358.30): C, 60.34; H, 4.22. Found: C, 59.99; H, 4.13.

4.4.10. 2-Heptafluoropropyl-6-hydroxy-4-methyl-benzoic acid methyl ester (**6j**)

Starting with silyl enol ether **4d** (0.619 g, 1.90 mmol), 1,3-bis-silyl enol ether **5a** (0.574 g, 2.20 mmol) and $TiCl_4$ (0.24 mL, 2.20 mmol), **6j** was isolated as a colourless solid (0.286 g, 45%), mp=85 °C. ^1H NMR (250 MHz, $CDCl_3$): δ=2.40 (s, 3H, ArCH_3), 3.91 (s, 3H, OCH_3), 7.00 (s, 1H, Ar), 7.03 (s, 1H, Ar), 9.78 (s, 1H, O*H*); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−121.1 (m, CF_2), −99.7 (m, CF_2), −80.7 (t, CF_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.6 (Ar*C*H_3), 52.6 (O*C*H_3), 111.1 (t, ^3J=2.5 Hz, *C*CO_2CH_3), 121.8 (t, ^3J=9.6 Hz, *C*HCC_3F_7), 121.9 (*C*HCOH), 129.1 (t, ^2J=23.6 Hz, *C*C_3F_7), 144.4 (*C*CH_3), 160.2 (*C*OH), 169.3 (*C*O); IR (ATR, cm^{-1}): ν=3300 (m), 1705 (s), 1615 (m), 1344 (s), 1300 (s), 1222 (s), 1198 (s), 1130 (m), 1111 (s); MS (EI, 70 eV): *m*/*z* (%)=334 (M^+, 25), 302 (100), 255 (9), 155 (59); HRMS (EI, 70 eV) calcd for $C_{12}H_9F_7O_3$ (M^+): 334.04344, found 334.04406. Anal. Calcd for $C_{12}H_9F_7O_3$ (334.19): C, 43.13; H, 2.71. Found: C, 43.13; H, 2.77.

Crystal data of **6j**. Empirical formula: $C_{12}H_9F_7O_3$. Formula weight: 334.19. Temperature: 173(2) K. Wavelength: 0.71073 Å. Crystal system: monoclinic. Space group (H.-M.): $P2_1/c$. Space group (Hall): −*P*2*ybc*. Unit cell dimensions: a=11.6397(4) Å, α=90°, b=10.1363(3) Å, β=100.016(2)°, c=11.2196(4) Å, γ=90°. Volume: 1303.55(8) $Å^3$; Z=4. Density (calculated): 1.703 Mg/m^3. Absorption coefficient: 0.185 mm^{-1}. F(000)=672. Crystal size: 0.48×0.38×0.11 mm^3. Θ Range for data collection: 2.68–30.00°. Index ranges: $-16\le h\le 16$, $-14\le k\le 14$, $-15\le l\le 15$. Reflections collected: 19,441. Independent reflections: 3799 [R(int)=0.0315]. Completeness to Θ=30.00°: 99.7%. Absorption correction: semi-empirical from equivalents. Max. and min. transmissions: 0.9800 and 0.9166. Refinement method: full-matrix least-squares on F^2. Data/restraints/parameters: 3799/0/205. Goodness-of-fit on F^2: 1.029. Final R indices [$I>2\sigma(I)$]: $R1$=0.0415, $wR2$=0.1061. R indices (all data): $R1$=0.0543, $wR2$=0.1170. Largest diff. peak and hole: 0.563 and −0.423 e/$Å^3$.

4.4.11. 3-Ethyl-6-heptafluoropropyl-2-hydroxy-4-methyl-benzoic acid methyl ester (**6k**)

Starting with silyl enol ether **4d** (0.436 g, 1.34 mmol), 1,3-bis-silyl enol ether **5d** (0.476 g, 1.65 mmol) and $TiCl_4$ (0.18 mL, 1.65 mmol), **6k** was isolated as a yellow liquid (0.314 g, 65%). ^1H NMR (250 MHz, $CDCl_3$): δ=1.14 (t, ^3J=7.5 Hz, 3H, CH_2CH_3), 2.38 (s, 3H, ArCH_3), 2.74 (q, ^3J=7.5 Hz, 2H, CH_2CH_3), 3.91 (s, 3H, OCH_3), 6.98 (s, 1H, Ar), 10.06 (s, 1H, O*H*); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−121.1 (m, CF_2), −99.4 (m, CF_2), −80.8 (t, CF_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=12.6 (CH_2CH_3), 19.7 (Ar*C*H_3), 19.9 (*C*H_2CH_3), 52.6 (O*C*H_3), 110.6 (t, ^3J=2.3 Hz, *C*CO_2CH_3), 122.3 (t, ^3J=9.6 Hz, *C*HCC_3F_7), 125.9 (t, ^2J=23.6 Hz, *C*C_3F_7), 135.5 (*C*CH_2CH_3), 141.8 (*C*CH_3), 158.2 (*C*OH), 170.0 (*C*O); IR (ATR, cm^{-1}): ν=2961 (w), 2879 (w), 1677 (m), 1607 (m), 1440 (m), 1348 (m), 1285 (m), 1223 (s), 1201 (s), 1181 (s), 1151 (m), 1106 (s), 952 (s); MS (EI, 70 eV): *m*/*z* (%)=362 (M^+, 38), 330 (100), 310 (26), 302 (20); HRMS (EI, 70 eV) calcd for $C_{14}H_{13}F_7O_3$ (M^+): 362.07474, found 362.07409.

4.4.12. 1-(2-Heptafluoropropyl-6-hydroxy-4-methyl-phenyl)-ethanone (**6l**)

Starting with silyl enol ether **4d** (0.414 g, 1.27 mmol), 1,3-bis-silyl enol ether **5b** (0.403 g, 1.65 mmol) and $TiCl_4$ (0.18 mL, 1.65 mmol), **6l** was isolated as a colourless solid (0.163 g, 40%), mp=109 °C. ^1H NMR (250 MHz, $CDCl_3$): δ=2.30 (s, 3H, CH_3), 2.51 (s, 3H, CH_3), 6.80 (s, 1H, Ar), 6.89 (s, 1H, Ar), 6.98 (s, 1H, O*H*); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−124.4 (m, CF_2), −104.7 (m, CF_2), −80.1 (t, CF_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.1 (Ar*C*H_3), 32.2 (*C*O*C*H_3), 120.7 (*C*HCOH), 120.8 (t, ^3J=7.3 Hz, *C*HCC_3F_7), 125.4 (t, ^2J=23.4 Hz, *C*C_3F_7),

126.3 (t, ^3J=2.8 Hz, $CCOCH_3$), 141.1 (CCH_3), 152.9 (COH), 205.1 (CO); IR (ATR, cm^{-1}): ν=3330 (m), 1694 (m), 1614 (m), 1342 (s), 1219 (s), 1198 (s), 1109 (s); MS (EI, 70 eV): m/z (%)=318 (M^+, 16), 303 (100), 255 (23), 155 (5); HRMS (EI, 70 eV) calcd for $C_{12}H_9F_7O_2$ (M^+): 318.04853, found 318.04879.

Crystallographic data of ***6l***. Empirical formula: $C_{12}H_9F_7O_2$. Formula weight: 318.19. Temperature: 173(2) K. Wavelength: 0.71073 Å. Crystal system: monoclinic. Space group (H.-M.): $P2_1/c$. Space group (Hall): $-P2ybc$. Unit cell dimensions: a=11.3509(4) Å, α=90°, b=10.9404(3) Å, β=99.845(2)°, c=10.2349(3) Å, γ=90°. Volume: 1252.29(7) Å; Z=4. Density (calculated): 1.688 Mg/m^3. Absorption coefficient: 0.182 mm^{-1}. F(000)=640. Crystal size: 0.35×0.31×0.17 mm^3. Θ Range for data collection: 2.60×30.00°. Index ranges: $-14\leq h\leq 15$, $-15\leq k\leq 14$, $-14\leq l\leq 13$. Reflections collected: 13,542. Independent reflections: 3646 [R(int)=0.0253]. Completeness to Θ=30.00°: 99.9%. Absorption correction: semi-empirical from equivalents. Max. and min. transmissions: 0.9698 and 0.9391. Refinement method: full-matrix least-squares on F^2. Data/restraints/parameters 3646/0/196. Goodness-of-fit on F^2: 1.039. Final R indices [$I>2\sigma(I)$]: $R1$=0.0379, $wR2$=0.1006. R indices (all data): $R1$=0.0482, $wR2$=0.1089. Largest diff. peak and hole: 0.402 and −0.273 e/Å^3

4.4.13. 1-(6-Heptafluoropropyl-2-hydroxy-3,4-dimethyl-phenyl)-propan-1-one (*6m*)

Starting with silyl enol ether **4d** (0.414 g, 1.27 mmol), 1,3-bis-silyl enol ether **5c** (0.450 g, 1.65 mmol) and $TiCl_4$ (0.18 mL, 1.65 mmol), **6m** was isolated as a pale yellow solid (0.163 g, 37%), mp=76 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.16 (t, ^3J=7.2 Hz, 3H, CH_2CH_3), 2.18 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 2.76 (q, ^3J=7.2 Hz, 2H, CH_2CH_3), 6.05 (s, 1H, OH), 6.95 (s, 1H, Ar); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−124.3 (m, CF_2), −104.5 (m, CF_2), −80.1 (t, CF_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=7.8 (CH_2CH_3), 11.9 ($ArCH_3$), 20.3 ($ArCH_3$), 38.1 (CH_2CH_3), 121.5–121.8 (m, $CHCC_3F_7$), 122.1 (t, ^2J=23.9 Hz, CC_3F_7), 126.8 (t, ^3J=2.9 Hz, $CCO_2CH_2CH_3$), 128.8 (CCH_3), 139.3 (CCH_3), 150.6 (COH), 207.9 (CO); IR (ATR, cm^{-1}): ν=3365 (m), 2980 (w), 2945 (w), 1698 (s), 1610 (m), 1350 (m), 1200 (s), 1100 (s); MS (EI, 70 eV): m/z (%)=346 (M^+, 11), 317 (100), 277 (9), 269 (29); HRMS (EI, 70 eV) calcd for $C_{14}H_{13}F_7O_2$ (M^+): 346.07983, found 346.08060. Anal. Calcd for $C_{14}H_{13}F_7O_2$ (346.24): C, 48.56; H, 3.78. Found: C, 48.79; H, 3.73.

4.4.14. 2-Heptafluoropropyl-6-hydroxy-4-propyl-benzoic acid methyl ester (*6n*)

Starting with silyl enol ether **4e** (0.709 g, 2.00 mmol), 1,3-bis-silyl enol ether **5a** (0.574 g, 2.20 mmol) and $TiCl_4$ (0.24 mL, 2.20 mmol), **6n** was isolated as a pale yellow solid (0.286 g, 40%), mp=56 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=0.95 (t, ^3J=7.3 Hz, 3H, CH_2CH_3), 1.57–1.74 (m, 2H, CH_2CH_3), 2.62 (t, ^3J=7.6 Hz, 2H, $ArCH_2$), 3.91 (s, 3H, OCH_3), 7.01 (s, 1H, Ar), 7.03 (s, 1H, Ar), 9.75 (s, 1H, OH); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−121.2 (m, CF_2), −99.8 (m, CF_2), −80.7 (t, CF_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=13.6 (CH_2CH_3), 23.7 (CH_2), 37.8 (CH_2), 52.6 (OCH_3), 111.3 (t, ^3J=2.2 Hz, CCO_2CH_3), 121.2 (CHCOH), 121.3 (t, ^3J=9.8 Hz, $CHCC_3F_7$), 129.0 (t, ^2J=23.3 Hz, CC_3F_7), 149.1 ($CCH_2CH_2CH_3$), 160.2 (COH), 169.3 (CO); IR (ATR, cm^{-1}): ν=3288 (m), 2963 (w), 2938 (w), 2878 (w), 1706 (s), 1615 (m), 1434 (m), 1342 (m), 1220 (s), 1201 (s), 1115 (s); MS (EI, 70 eV): m/z (%)=362 (M^+, 26), 330 (100), 302 (88), 273 (35); HRMS (EI, 70 eV) calcd for $C_{14}H_{13}F_7O_3$ (M^+): 362.07474, found 362.07454.

4.4.15. 1-(6-Heptafluoropropyl-2-hydroxy-3-methyl-4-propyl-phenyl)-propan-1-one (*6o*)

Starting with silyl enol ether **4e** (0.709 g, 2.00 mmol), 1,3-bis-silyl enol ether **5c** (0.600 g, 2.20 mmol) and $TiCl_4$ (0.24 mL, 2.20 mmol), **6o** was isolated as a pale yellow solid (0.229 g, 31%), mp=63 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=0.97 (t, ^3J=7.3 Hz, 3H, $CH_2CH_2CH_3$), 1.16 (t, ^3J=7.2 Hz, 3H, $COCH_2CH_3$), 1.49–1.66 (m, 2H, $CH_2CH_2CH_3$), 2.21 (s, 3H, $ArCH_3$), 2.61 (t, ^3J=7.7 Hz, 2H, $ArCH_2$), 2.77 (q, ^3J=7.2 Hz, 2H, $COCH_2$), 6.03 (s, 1H, OH), 6.94 (s, 1H, ArH); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−124.4 (m, CF_2), −104.7 (m, CF_2), −80.1 (t, CF_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=7.9 (CH_3), 11.5 (CH_3), 13.8 (CH_3), 23.2 (CH_2), 35.7 (CH_2), 38.1 (CH_2), 121.2 (t, ^3J=7.2 Hz, $CHCC_3F_7$), 122.2 (t, ^2J=23.5 Hz, CC_3F_7), 126.5 (t, ^3J=2.8 Hz, $CCOCH_2CH_3$), 128.2 (C), 143.6 (C), 150.8 (COH), 207.8 (CO); IR (ATR, cm^{-1}): ν=3379 (m), 2963 (w), 2936 (w), 2876 (w), 1702 (m), 1608 (w), 1572 (w), 1353 (m), 1223 (s), 1199 (s), 1109 (s); MS (EI, 70 eV): m/z (%)=374 (M^+, 10), 345 (100), 297 (13), 227 (4); HRMS (EI, 70 eV) calcd for $C_{16}H_{17}F_7O_2$ (M^+): 374.11113, found 374.11086.

4.4.16. 4-Heptafluoropropyl-6-hydroxy-indane-5-carboxylic acid methyl ester (*6p*)

Starting with silyl enol ether **4f** (0.705 g, 2.00 mmol), 1,3-bis-silyl enol ether **5a** (0.573 g, 2.20 mmol) and $TiCl_4$ (0.24 mL, 2.20 mmol), **6p** was isolated as a colourless solid (0.294 g, 41%), mp=90 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.98–2.11 (m, 2H, $ArCH_2CH_2$), 2.89 (t, ^3J=7.5 Hz, 2H, $ArCH_2$), 3.02 (t, ^3J=7.4 Hz, 2H, $ArCH_2$), 3.88 (s, 3H, CH_3), 7.04 (s, 1H, ArH), 8.37 (s, 1H, OH); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−120.1 (m, CF_2), −99.5 (m, CF_2), −80.8 (t, CF_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=25.4 (CH_2), 32.8 (CH_2), 32.9 (CH_2), 52.7 (CH_3), 114.2 (t, ^3J=4.2 Hz, CCC_3F_7), 117.1 (CHCOH), 124.2 (t, ^2J=23.5 Hz, CC_3F_7), 137.2 (t, ^3J=4.3 Hz, CCC_3F_7), 151.7 (CCHCOH), 156.8 (COH), 169.6 (CO); IR (ATR, cm^{-1}): ν=3359 (m), 2966 (w), 2956 (w), 2873 (w), 1712 (s), 1608 (m), 1441 (m), 1342 (m), 1284 (s), 1239 (s), 1215 (s), 1195 (s), 1167 (s), 1106 (s), 962 (s), 950 (s), 732 (s); MS (EI, 70 eV): m/z (%)=360 (M^+, 16), 328 (100), 209 (8), 181 (24); HRMS (EI, 70 eV) calcd for $C_{14}H_{11}F_7O_3$ (M^+): 360.05909, found 360.05893. Anal. Calcd for $C_{14}H_{11}F_7O_3$ (360.22): C, 46.68; H, 3.08. Found: C, 46.79; H, 2.94.

4.4.17. 5-Heptafluoropropyl-3-hydroxy-biphenyl-4-carboxylic acid methyl ester (*6q*)

Starting with silyl enol ether **4g** (1.165 g, 3.00 mmol), 1,3-bis-silyl enol ether **5a** (0.860 g, 3.30 mmol) and $TiCl_4$ (0.36 mL, 3.30 mmol), **6q** was isolated as a colourless solid (0.560 g, 47%), mp=84 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=3.96 (s, 3H, OCH_3), 7.40–7.64 (m, 7H, ArH), 9.85 (s, 1H, OH); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−121.1 (m, CF_2), −99.8 (m, CF_2), −80.7 (q, CF_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=52.8 (OCH_3), 112.3 (t, ^3J=2.2 Hz, CCO_2CH_3), 119.7 (t, ^3J=9.6 Hz, $CHCC_3F_7$), 119.7 (CHCOH), 127.2 (Ph), 129.0 (Ph), 129.1 (Ph), 129.8 (t, ^2J=23.5 Hz, CC_3F_7), 138.2 (C), 146.3 (C), 160.4 (COH), 169.2 (CO); IR (ATR, cm^{-1}): ν=3290 (m), 3090 (w), 3062 (w), 3042 (w), 1699 (s), 1615 (m), 1574 (m), 1437 (m), 1414 (m), 1349 (s), 1311 (s), 1284 (s), 1223 (s), 1187 (s), 1149 (m), 1110 (s), 984 (m); MS (EI, 70 eV): m/z (%)=396 (M^+, 38), 364 (100), 336 (13), 217 (43), 188 (12), 109 (12); HRMS (EI, 70 eV) calcd for $C_{17}H_{11}F_7O_3$ (M^+): 396.05909, found 396.05970. Anal. Calcd for $C_{17}H_{11}F_7O_3$ (396.26): C, 51.53; H, 2.80. Found: C, 51.68; H, 2.87.

Crystallographic data of ***6l***. Empirical formula: $C_{17}H_{11}F_7O$. Formula weight: 396.26. Temperature: 173(2) K. Wavelength: 0.71073 Å. Crystal system: monoclinic. Space group (H.-M.): $P2_1/c$. Space group (Hall): $-P2ybc$. Unit cell dimensions: a=14.2740(3) Å, α=90°, b=8.9786(2) Å, β=92.3180(10)°, c=13.1741(3) Å, γ=90°. Volume: 1687.02(6) Å^3; Z=4. Density (calculated): 1.560 Mg/m^3. Absorption coefficient: 0.157 mm^{-1}. F(000)=800. Crystal size: 0.42×0.35×0.23 mm^3. Θ Range for data collection: 2.68–30.00°. Index ranges: $-20\leq h\leq 19$, $-12\leq k\leq 12$, $-18\leq l\leq 18$. Reflections collected: 38,562. Independent reflections: 4903 [R(int)=0.0226]. Completeness to Θ=30.00°: 99.3%. Absorption correction: semi-empirical from equivalents. Max. and min. transmissions: 0.9649 and 0.9372. Refinement method: full-matrix least-squares on F^2. Data/restraints/parameters: 4903/0/249. Goodness-of-fit on F^2: 1.033. Final R indices [$I>2\sigma(I)$]: $R1$=0.0408, $wR2$=0.1044. R indices

(all data): $R1$=0.0522, $wR2$=0.1146. Largest diff. peak and hole: 0.453 and −0.306 e/Å^3.

4.4.18. 2-Hydroxy-4-methyl-6-tridecafluorohexyl-benzoic acid methyl ester (**6r**)

Starting with silyl enol ether **4h** (0.703 g, 1.48 mmol), 1,3-bis-silyl enol ether **5a** (0.430 g, 1.65 mmol) and $TiCl_4$ (0.18 mL, 1.65 mmol), **6r** was isolated as a colourless solid (0.297 g, 42%), mp=106 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=2.39 (s, 3H, ArCH_3), 3.91 (s, 3H, OCH_3), 7.01 (s, 1H, Ar), 7.03 (s, 1H, Ar), 9.71 (s, 1H, O*H*); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−126.1 (m, CF_2), −122.7 (m, CF_2), −122.2 (m, CF_2), −117.1 (m, CF_2), −99.4 (m, CF_2), −80.8 (t, CF_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.6 (ArCH_3), 52.6 (OCH_3), 111.2 (t, ^3J=2.2 Hz, CCO_2CH_3), 121.9 (*C*HCOH), 122.1 (t, ^3J=9.5 Hz, $CHCC_6F_{13}$), 129.2 (t, ^2J=23.3 Hz, CC_6F_{13}), 144.4 (*C*CH$_3$), 160.1 (*C*OH), 169.3 (*C*O); IR (ATR, cm^{-1}): ν=3306 (w), 2924 (w), 2855 (w), 1706 (m), 1615 (w), 1438 (w), 1362 (w), 1302 (m), 1283 (m), 1234 (m), 1194 (s), 1176 (s), 1145 (s), 1134 (s), 1093 (m), 1067 (m); MS (EI, 70 eV): *m*/*z* (%)=484 (M$^+$, 14), 452 (100), 433 (7), 405 (5), 155 (62); HRMS (EI, 70 eV) calcd for $C_{15}H_9F_{13}O_3$ (M$^+$): 484.03386, found 484.03389.

4.4.19. 1-(2-Hydroxy-4-methyl-6-tridecafluorohexyl-phenyl)-ethanone (**6s**)

Starting with silyl enol ether **4h** (0.708 g, 1.49 mmol), 1,3-bis-silyl enol ether **5b** (0.403 g, 1.65 mmol) and $TiCl_4$ (0.18 mL, 1.65 mmol), **6s** was isolated as a pale red solid (0.288 g, 41%), mp=122 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=2.35 (s, 3H, CH_3), 2.52 (s, 3H, CH_3), 6.31 (s, 1H, O*H*), 6.86 (s, 1H, Ar), 6.95 (s, 1H, Ar); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−126.1 (m, CF_2), −122.8 (m, CF_2), −121.6 (m, CF_2), −119.6 (m, CF_2), −103.5 (m, CF_2), −80.8 (t, CF_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.1 (ArCH_3), 32.2 (COCH_3), 120.5 (t, ^3J=7.6 Hz, *C*HCC$_6$F$_{13}$), 121.1 (*C*HCOH), 125.7 (t, ^2J=23.3 Hz, CC_6F_{13}), 128.8 (t, ^3J=3.3 Hz, $CCOCH_3$), 141.5 (*C*CH$_3$), 154.8 (*C*OH), 201.4 (*C*O); IR (ATR, cm^{-1}): ν=3287 (w), 2963 (w), 2932 (w), 1694 (m), 1615 (w), 1361 (w), 1322 (m), 1282 (w), 1231 (m), 1190 (m), 1178 (m), 1136 (m), 1067 (m); MS (EI, 70 eV): *m*/*z* (%)=468 (M$^+$, 12), 453 (100), 405 (10); HRMS (EI, 70 eV): calcd for $C_{15}H_9F_{13}O_2$ (M$^+$): 468.03895, found 468.03843. Anal. Calcd for $C_{15}H_9F_{13}O_2$ (468.21): C, 38.48; H, 1.94. Found: C, 38.31; H, 1.92.

4.4.20. 1-(2-Hydroxy-3-methyl-6-pentadecafluoroheptyl-4-propyl-phenyl)-propan-1-one (**6t**)

Starting with silyl enol ether **4i** (0.930 g, 1.68 mmol), 1,3-bis-silyl enol ether **5c** (0.600 g, 2.20 mmol) and $TiCl_4$ (0.24 mL, 2.20 mmol), **6t** was isolated as a yellow solid (0.398 g, 41%), mp=83 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=0.97 (t, ^3J=7.3 Hz, 3H, $CH_2CH_2CH_3$), 1.17 (t, ^3J=7.2 Hz, 3H, $COCH_2CH_3$), 1.50–1.67 (m, 2H, $CH_2CH_2CH_3$), 2.22 (s, 3H, ArCH_3), 2.62 (t, ^3J=7.7 Hz, 2H, ArCH_2), 2.79 (q, ^3J=7.2 Hz, 2H, COCH_2), 5.87 (s, 1H, O*H*), 6.95 (s, 1H, Ar*H*); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−126.1 (m, CF_2), −122.7 (m, CF_2), −122.0 (m, CF_2), −121.4 (m, CF_2), −119.8 (m, CF_2), −103.9 (m, CF_2), −80.8 (t, CF_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=7.9 (*C*H$_3$), 11.5 (*C*H$_3$), 13.8 (*C*H$_3$), 23.2 (*C*H$_2$), 35.8 (*C*H$_2$), 38.1 (*C*H$_2$), 121.3 (t, ^3J=7.53 Hz, *C*HCC$_7$F$_{15}$), 122.4 (t, ^2J=23.4 Hz, CC_7F_{15}), 126.5 (t, ^3J=2.7 Hz, $CCOCH_2CH_3$), 128.1 (*C*), 143.6 (*C*), 150.8 (*C*OH), 207.7 (*C*O); IR (ATR, cm^{-1}): ν=3265 (w), 2967 (w), 2944 (w), 2879 (w), 1693 (m), 1606 (w), 1571 (w), 1316 (w), 1233 (m), 1194 (s), 1139 (m), 1129 (s), 1113 (m), 1101 (m), 1014 (m); MS (EI, 70 eV): *m*/*z* (%)=574 (M$^+$, 5), 545 (100), 497 (12); HRMS (EI, 70 eV): calcd for $C_{20}H_{17}F_{15}O_2$ (M$^+$): 574.09843, found 574.09733.

4.4.21. 1-(6-Hydroxy-7-methyl-4-pentadecafluoroheptyl-indan-5-yl)-propan-1-one (**6u**)

Starting with silyl enol ether **4j** (0.730 g, 1.32 mmol), 1,3-bis-silyl enol ether **5c** (0.450 g, 1.65 mmol) and $TiCl_4$ (0.18 mL, 1.65 mmol), **6u** was isolated as a yellow solid (0.227 g, 30%), mp=167 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.09 (t, ^3J=7.2 Hz, 3H, CH_2CH_3), 1.99–2.14 (m, 2H, $ArCH_2CH_2$), 2.26 (s, 3H, ArCH_3), 2.77 (q, ^3J=7.2 Hz, 2H, CH_2CH_3), 2.88 (t, ^3J=7.4 Hz, 2H, ArCH_2), 3.02 (t, ^3J=7.4 Hz, 2H, ArCH_2), 7.95 (s, 1H, O*H*); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−125.8 (m, CF_2), −122.3 (m, CF_2), −121.5 (m, CF_2), −121.3 (m, CF_2), −118.4 (m, CF_2), −102.5 (m, CF_2), −80.8 (t, CF_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=7.9 (*C*H$_3$), 13.2 (*C*H$_3$), 25.7 (*C*H$_2$), 32.2 (*C*H$_2$), 33.8 (*C*H$_2$), 38.2 (*C*H$_2$), 118.4 (t, ^2J=23.7 Hz, CC_7F_{15}), 127.6 (*C*), 131.4 (t, ^3J=4.4 Hz, CCC_7F_{15}), 136.4 (t, ^3J=4.1 Hz, CCC_7F_{15}), 147.7 (*C*), 151.1 (*C*OH), 204.9 (*C*O); IR (ATR, cm^{-1}): ν=3333 (w), 2984 (w), 2943 (w), 2881 (w), 1698 (m), 1583 (w), 1367 (w), 1288 (w), 1238 (m), 1198 (s), 1142 (s), 1127 (m), 1097 (m); MS (EI, 70 eV): *m*/*z* (%)=572 (M$^+$, 18), 543 (100), 503 (13), 495 (25); HRMS (EI, 70 eV) calcd for $C_{20}H_{15}F_{15}O_2$ (M$^+$): 572.08270, found 572.08315.

4.4.22. 3-Hydroxy-5-pentadecafluoroheptyl-biphenyl-4-carboxylic acid methyl ester (**6v**)

Starting with silyl enol ether **4k** (1.177 g, 2.00 mmol), 1,3-bis-silyl enol ether **5a** (0.573 g, 2.20 mmol) and $TiCl_4$ (0.24 mL, 2.20 mmol), **6v** was isolated as a colourless solid (0.424 g, 36%), mp=113 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=3.96 (s, 3H, OCH_3), 7.37–7.66 (m, 7H, Ar*H*), 9.75 (s, 1H, O*H*); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−126.1 (m, CF_2), −122.7 (m, CF_2), −121.9 (m, 4F, CF_2), −117.0 (m, CF_2), −99.4 (m, CF_2), −80.8 (t, CF_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=52.8 (OCH_3), 112.7 (t, ^3J=2.2 Hz, CCO_2CH_3), 119.7 (*C*HCOH), 119.8 (t, ^3J=9.8 Hz, $CHCC_7F_{15}$), 127.2 (Ph), 129.0 (Ph), 129.1 (Ph), 129.8 (t, ^2J=23.4 Hz, CC_7F_{15}), 138.3 (*C*), 146.2 (*C*), 160.2 (*C*OH), 169.1 (*C*O); IR (ATR, cm^{-1}): ν=3400 (w), 3085 (w), 3061 (w), 3040 (w), 3011 (w), 2959 (w), 1711 (m), 1614 (m), 1410 (m), 1307 (m), 1277 (m), 1240 (m), 1191 (s), 1140 (s), 1126 (s), 1098 (m), 1062 (m), 1026 (m); MS (EI, 70 eV): *m*/*z* (%)=596 (M$^+$, 22), 564 (100), 536 (13), 217 (82), 188 (13); HRMS (EI, 70 eV) calcd for $C_{21}H_{11}F_{15}O_3$ (M$^+$): 596.04632, found 596.04696.

4.4.23. 1-(3-Hydroxy-2-methyl-5-pentadecafluoroheptyl-biphenyl-4-yl)-propan-1-one (**6w**)

Starting with silyl enol ether **4k** (1.177 g, 2.00 mmol), 1,3-bis-silyl enol ether **5c** (0.600 g, 2.20 mmol) and $TiCl_4$ (0.24 mL, 2.20 mmol), **6w** was isolated as a pale red solid (0.600 g, 49%), mp=126 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.22 (t, ^3J=7.3 Hz, 3H, CH_2CH_3), 2.21 (s, 3H, ArCH_3), 2.85 (q, ^3J=7.3 Hz, 2H, CH_2CH$_3$), 5.84 (s, 1H, O*H*), 7.09 (s, 1H, Ar*H*), 7.23–7.50 (m, 5H, Ph*H*); ^{19}F NMR (235 MHz, $CDCl_3$): δ=−126.1 (m, CF_2), −122.7 (m, CF_2), −122.0 (m, CF_2), −121.4 (m, CF_2), −119.7 (m, CF_2), −104.1 (m, CF_2), −80.8 (t, CF_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=7.8 (*C*H$_3$), 13.4 (*C*H$_3$), 38.1 (*C*H$_2$), 122.0 (t, ^3J=7.4 Hz, $CHCC_7F_{15}$), 122.8 (t, ^2J=23.9 Hz, CC_7F_{15}), 127.5 (*C*), 127.7 (*C*), 127.9 (Ph), 128.4 (Ph), 129.0 (Ph), 139.6 (*C*), 144.3 (*C*), 151.0 (*C*OH), 206.9 (*C*O); IR (ATR, cm^{-1}): ν=3412 (w), 3055 (w), 2986 (w), 2944 (w), 2906 (w), 2884 (w), 1704 (m), 1599 (w), 1564 (w), 1204 (s), 1142 (s), 1128 (s), 1099 (m); MS (EI, 70 eV): *m*/*z* (%)=608 (M$^+$, 30), 579 (100), 531 (56), 262 (24); HRMS (EI, 70 eV) calcd for $C_{23}H_{15}F_{15}O_2$ (M$^+$): 608.08270, found 608.08305.

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22. CCDC 689114–689118 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.