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Nucleophilic difluoromethylenation of aldehydes and ketones using diethyl difluoro(trimethylsilyl)methylphosphonate

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ABSTRACT

A new nucleophilic difluoromethylenation of aldehydes and ketones using diethyl difluoro(trimethylsilyl)methylphosphonate (**1**) has been achieved. The reactive carbanion species were generated under mild reaction conditions with a catalytic amount of initiator. This methodology was compatible with non-enolizable and in some cases with enolizable aldehydes and ketones and provided a straightforward access to phosphates of *syn* and *anti* 2,2-difluoro-1,3-diols.

1. Introduction

Nucleophilic difluoromethylation is an important synthetic strategy for the introduction of the CF_2 group into organic compounds and thereby expansion of the diversity of available selectively fluorinated compounds useful in drug design and material research.

Previously, nucleophilic difluoromethylation has been achieved using sulfur [1] and selenium [2] containing reagents. For the nucleophilic installation of difluoromethylene group $PhSO_2CF_2H$ was used as a $[CF_2]^{2-}$ equivalent [3] and $PhSCF_2TMS$ as a $[CF_2]^{-}$ equivalent [4].

Recently, we have reported the use of diethyl difluoromethylphosphonate (**2**) for the nucleophilic difluoromethylation and difluoromethylenation of aldehydes and ketones. Utilization of phosphonate **2** gave access to a variety of CF_2 containing compounds such as 2,2-difluoroethan-1-ols and their phosphates, 2,2-difluoro-1,3-diols and their phosphates [5], and also to substituted flurovinyl phosphates [6]. However, there were some drawbacks: the employment of strong bases such as *t*-BuOK in nucleophilic difluoromethylenation reactions prohibited the use of enolizable carbonyl compounds and required isolation of intermediate phosphonates.

In this article we wish to report the use of diethyl difluoro(trimethylsilyl)methylphosphonate (**1**) as a new $[CF_2]^{2-}$ synthon for the difluoromethylenation of aldehydes and ketones. We were particularly intrigued by the possibility of base-free generation of (diethylphosphinyl)difluoromethyl carbanion under mild conditions (with only catalytic amount of initiator) and consecutive multistep conversions to difluoromethylene containing products in "one-pot".

A number of initiators are known for the generation of fluorinated carbanions from the trimethylsilyl precursors such as CF_3TMS [7], $PhSO_2CF_2TMS$ [8], $PhSCF_2TMS$ [1b] [4]. They include fluoride source (CsF, TBAF, TBAT [9]), oxygen anions (metal alkoxides, carboxylic acid salts, potassium carbonate, phosphate salts [10], triethylamine *N*-oxide [11]), Lewis bases (Et_3N, pyridine, PPh_3, $AsPh_3$, $SbPh_3$) [12] and N-heterocyclic carbenes [13].

Phosphonates containing the trimethylsilyl group are known and their chemistry has been investigated [14]. Fluorinated phosphonates [15] with a TMS group have also received some attention. Phosphonate **1** was used for the synthesis of 1,1-difluoro-2-hydroxyalkylphosphonates by the reaction of carbonyl compounds using catalytic amount of CsF [16] or TBAF [17]. Toru and co-workers have used excess of **1** and TMAF to transform an aromatic aldehyde into a difluoromethyl containing phosphate [18]. Phosphonate **1** was also used for the preparation of ^{14}C labeled difluoroethene starting from ^{14}C formaldehyde followed by a modification of Wadsworth–Emmons reaction [19].

2. Results and discussion

At the outset of our study we have optimized reaction conditions the type and amount of initiator for the formation of

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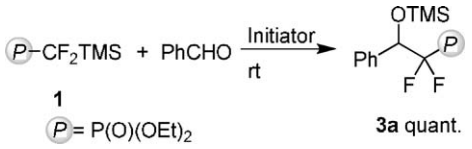
Table 1
Formation of **3a** from **1** and benzaldehyde[a].



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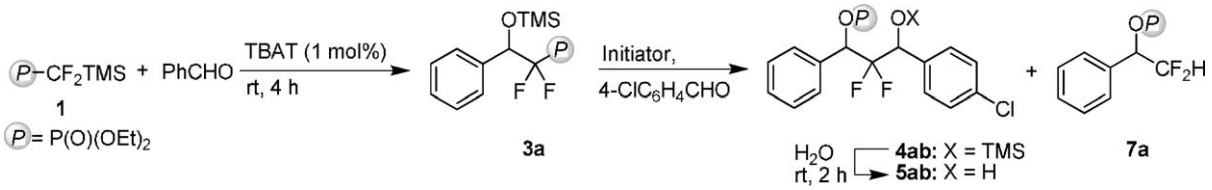
Entry	Initiator (mol%)	Time	Solvent
1	KF (5)	15 h	DMF
2	K_2CO_3 (100)	1 h	DMF
3	K_2CO_3 (1)	24 h	DMF
4	TBAT (1)	4 h	DMF
5	TBAT (1)	4 h	THF

[a]All reactions were performed with PhCHO (1 equiv) at rt and lead to the product **3a** in quantitative GC yield.

phosphonate **3a** (R^1 = Ph, R^2 = H) using diethyl difluoro(trimethylsilyl)methylphosphonate (**1**) [20] and benzaldehyde. The results of optimization are summarized in Table 1.

Potassium fluoride (entry 1) was found to be very slow initiator. The reaction with 1 equiv of potassium carbonate was fast and clean, however because of the basic character of this activator the reaction mixture could not be used for further conversions without isolation of **3a** as intended. With catalytic potassium carbonate the reaction was very slow. Contrary to the literature [16], the employment of CsF (5 mol%) in THF gave only traces of **3a** after 20 h. It is interesting to mention that switching to DMF as a solvent gave a mixture of **3a**, **4a** and **5a**. TBAT was identified as an initiator of choice, because of its low basicity, good solubility in organic solvents and non-hydroscopic nature. With only 1 mol% of TBAT the reaction was finished in 4 h giving the product **3a** in 94% isolated yield without the need of chromatographic separation. Similarly **3e** was prepared starting

Table 2
Optimization of reaction conditions for the formation of **5ab** from **1** or **3a**[a].



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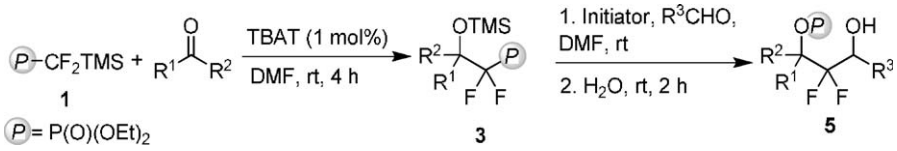
Entry	Initiator (mol%)	Method	Solvent	Temperature	Time	Yield **5ab** (%)[b]	Yield **7a** (%)[b]
1	CsF (100)	*A*	DMF	−30 °C to 0 °C	2 h	85	15
2	CsF (50)	*B*	DMF	−50 °C to 0 °C	4 h	94	6
3	TBAT (100)	*B*	DMF	0 °C to rt	4 h	90	10
4	TBAT (50)	*C*	DMF	0 °C to rt	15 h	78	22
5	TBAT (30)	*B*	DMF	rt	3 h	98	2
6	TBAT (30)	*B*	DMF	40 °C	1 h	98	2
7	TBAT (30)	*B*	THF	rt	15 h	89	11
8	TBAT (10)	*B*	DMF	40 °C	4 d	94	4

[a] Reaction conditions (solvent, temp. and reaction time) shown in table refer to the formation of **4ab** and **5ab** from **3a**.
[b] Determined by GC–MS analysis.
Method *A*: To the solution of **3a** prepared in situ 4-ClC_6H_4CHO (2 equiv) and initiator were added.
Method *B*: Solution of **3a** prepared in situ was added to the mixture of 4-ClC_6H_4CHO (2 equiv) and initiator.
Method *C*: Initiator was added to the mixture of **3a** and 4-ClC_6H_4CHO (2 equiv).

Table 3
Difluoromethylenation of aldehydes leading to phosphates **5**[a].



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Entry	R^1	R^2	R^3	Method	Initiator (mol%)	Time	Yield **5** (%)[b]
1	Ph	H	4-ClC_6H_4	*B*	TBAT (30)	3 h	**5ab** 84
2	Ph	H	4-MeC_6H_4	*B*	CsF (50)	1 h	**5ac** 73
3	4-ClC_6H_4	H	4-$MeOC_6H_4$	*B*	CsF (50)	1.5 h	**5bd** 68
4	Ph	H	*n*-C_6H_{13}	*C*	TBAT (50)	1 h	**5ae** 70[c]
5	*n*-C_6H_{13}	H	Ph	*C*	CsF (50)	3 h	**5ea** 64
6	*n*-C_6H_{13}	H	4-ClC_6H_4	*C*	CsF (50)	3 h	**5eb** 62
7	Me	Me	4-ClC_6H_4	*C*	CsF (50)	4 h	**5fb** 56

[a] Reaction conditions (solvent, temp. and reaction time) shown in table refer to the formation of **5** from **3**.
[b] Isolated yields unless noted otherwise.
[c] Determined by GC–MS analysis. Side-product **7a** (30%) was also formed.
Method *B*: Solution of **3** prepared in situ was added to the mixture of R^3CHO (2 equiv) and initiator.
Method *C*: Initiator was added to the mixture of **3** and R^3CHO (2 equiv).

from *n*-heptanal in 93% isolated yield[1] and **3f** from acetone in 85% yield.

Having identified optimal reaction conditions for the formation of **3**, we turned our attention to difluoromethylenation. Again some optimization of reaction conditions was needed. We have used benzaldehyde in the first step (formation of **3a**) and 4-chlorobenzaldehyde in the second step leading to difluoromethylene containing phosphates **4ab** and **5ab**. We have started either from isolated **3a** or prepared in situ from **1** and benzaldehyde using conditions described in Table 1, entries 4 and 5. Results are shown in Table 2.

As shown in Table 2, CsF or TBAT were identified as efficient initiators. This time the required amount of initiator was 0.3–1 equiv. With lower amount of initiator the reactions was found to be very slow (entry 8). The product was formed as a mixture of TMS protected alcohol **4ab** and free alcohol **5ab**. Compound **4ab** can be smoothly converted into **5ab** by the addition of small amounts of water. We avoided the use of more common TBAF reagent for the removal of TMS moiety, because the fluoride ion also attacked phosphorus atom giving rise to neurotoxin diethyl phosphorofluoridate (detected by GC–MS). The starting phosphonate **3a** was prepared in situ, the second aldehyde together with initiator were added subsequently (method *A*). Alternatively, reversed addition was used (method *B*). In method *C* isolated **3a** was used as a starting phosphonate. The by-product phosphate **7a** was observed in all cases; however its formation can be minimized using method *B*. The most efficient formation of **5ab** was observed using conditions shown in entries 2, 5 and 6.

Results of preparative synthesis of phosphates **5** are presented in Table 3.

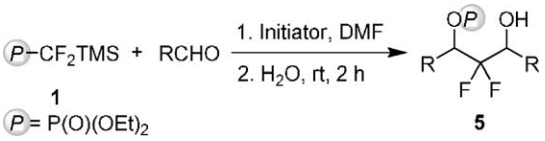
In reactions where R^3CHO is an activated aldehyde, such as 4-chlorobenzaldehyde, TBAF works as efficient activator (entry 1). However the application of TBAT in the case of non-activated aryl aldehydes (such as 4-methyl or 4-methoxy benzaldehyde) gave very slow conversion to the product **5** and formation of significant amount of by-product **7**. The use of CsF on the other hand was found to be successful (entries 2 and 3). The application of enolizable aldehydes was met with limited success. Phosphonate **3a** with *n*-heptanal in the presence of TBAT gave the desired phosphate, however large amount of by-product **7a** was formed (entry 4). Starting from phosphonate **3e** and various aryl aldehydes (entries 5 and 6) the desired phosphates could be isolated in good yields in the presence of CsF. With TBAT only TMS group deprotection of **3e** was observed. Moderate yield of phosphate **5fb** was obtained starting from phosphonate **3f** derived from acetone and activated aldehyde (entry 7).

Products **5** were formed as a mixture of *syn* and *anti* isomers in 1:1 ratio. These isomers were conveniently separated on silica gel column chromatography and characterized individually. During the formation of phosphates **5** migration of phosphorus group from one oxygen atom to the other took place and the products are mixtures of isomeric phosphates in different ratios as mentioned in our previous study [5a]. Phosphate moiety of **5** can be conveniently removed affording 2,2-difluoro-1,3-diols [5a].

Application of an excess of aromatic aldehyde in the reaction with **1** and initiator (TBAT for activated aldehydes and CsF for less reactive ones) gave rise to phosphates **5** of symmetrical diols in one step and very good yields (Table 4, entries 1–4). The use of enolizable aldehyde (*n*-heptanal) gave only low GC yield of the desired product **5ee** together with significant amounts of by-products **2**, **3e** and **7e** (entry 5). With ketones such as acetone or acetophenone no difluromethylene containing products were observed.

[1] *Cis* and *trans* TMS enols of *n*-heptanal and **2** were detected as side products in ca. 5% yield.

Table 4
Difluoromethylenation of aldehydes leading to phosphates **5** of symmetrical diols[a].



Entry	R	Initiator (50 mol%)	Temperature	Time	Yield **5** (%)[b]
1	Ph	TBAT	0 °C to rt	5 h	**5aa** 89
2	4-ClC_6H_4	TBAT	0 °C to rt	2 h	**5bb** 77
3	4-MeC_6H_4	CsF	−5 °C to rt	2 h	**5cc** 83
4	4-$MeOC_6H_4$	CsF	−5 °C to rt	4 h	**5dd** 79
5	*n*-C_6H_{13}	TBAT	−50 °C to rt	15 h	**5ee** 23[c]

[a] All reactions were performed with **1**, RCHO (4 equiv) and initiator in DMF.
[b] Isolated yields unless noted otherwise.
[c] Determined by GC–MS analysis. Side-products **2**, **3e**, **7e**, and products of enolization and aldol reaction of *n*-heptanal were also formed.

3. Conclusion

In conclusion we have developed a new method for nucleophilic difluoromethylenation of aldehydes and ketones using diethyl difluoro(trimethylsilyl)methylphosphonate (**1**). In contrast to previously described diethyl difluoromethylphosphonate (**2**), where low temperatures and excess of strong bases were needed, the application of TMS containing phosphonate **1** allowed the generation of (diethylphosphinyl)difluoromethyl carbanion under mild conditions with catalytic amount of fluoride initiator, giving rise to 1,1-difluoro-2-alkyl-2-(trimethylsilyloxy)ethylphosphonates (**3**) and phosphates of 2,2-difluoro-1,3-diols **5** in respectable yields. Starting from aryl aldehydes phosphates **5** of symmetrical diols were prepared in a single step, phosphates **5** of unsymmetrical diols in a reaction sequence from in situ preformed phosphonates **3** and in case of enolizable aldehydes and ketones from isolated **3**.

4. Experimental

^1H, ^{13}C, ^{19}F and ^{31}P NMR spectra were recorded in $CDCl_3$ on a Bruker 400 MHz instrument at 400, 100.6, 470 and 202 MHz. Chemical shifts (δ) are reported in ppm relative to Me_4Si (0 ppm, for ^1H NMR), residual $CHCl_3$ (7.26 ppm for ^1H NMR and 77.0 ppm for ^{13}C NMR), internal $CFCl_3$ (0 ppm for ^{19}F NMR), internal $(MeO)_3PO$ (3.0 ppm for ^{31}P NMR) and external H_3PO_4 in water (0 ppm for ^{31}P NMR). GC–MS spectra were recorded on an Agilent 7890A gas chromatograph coupled with 5975C quadrupole mass selective electron impact (EI) detector (70 eV). High resolution mass spectra (HRMS) were recorded on a LTQ Orbitrap XL instrument using electrospray (ESI) ionization. Infrared spectra were measured on a FTIR instrument. Reactions were conducted under Ar. DMF was dried by refluxing with calcium hydride followed by distillation and kept over molecular sieves (3 Å). THF was dried by distillation over Na/benzophenone. Aldehydes were distilled before use. Cesium fluoride was dried (0.1 torr, 250 °C, 1 h). All other chemicals were used as received.

4.1. Preparation of diethyl difluoro(trimethylsilyl)methylphosphonate (1) [20]

A solution of *n*-BuLi (23.4 mL, 2.5 M, 58.5 mmol) in petrol ether was added dropwise to a stirred solution of *i*-Pr_2NH (5.92 g, 58.5 mmol) in THF (100 mL) cooled to −78 °C. The reaction mixture was warmed up to 0 °C, stirred for 5 min, and again cooled down to −78 °C. A solution of diethyl difluoromethylphosphonate

(**2**) (10.0 g, 53.2 mmol) in THF (50 mL) was added dropwise, followed by stirring at this temperature for 30 min. A solution of TMSCl (8.69 g, 79.8 mmol) in THF (50 mL) was added, the mixture was stirred for 40 min at −78 °C and then warmed up to rt. The reaction mixture was poured into a solution of phosphoric acid (4.2 g, 85% aqueous) in water/ice (350 mL). The organic layer was separated and the aqueous layer was extracted with petrol ether (2 × 200 mL). Organic phases were combined, washed with brine (50 mL), dried ($MgSO_4$), filtered, concentrated under reduced pressure and purified by distillation (85–86 °C, 0.2 torr) affording the pure product as a colorless liquid (12.14 g, 88%): ^{1}H NMR: δ 0.27 (s, 9H, Si*Me*$_3$), 1.37 (t, 6H, $^3J_{HH}$ = 7.1 Hz, 2 × C*H*$_3$), 4.25 (dq, 4H, $^3J_{HP}$ = 7.4 Hz, $^3J_{HH}$ = 7.1 Hz, 2 × C*H*$_2$); ^{13}C NMR: δ −4.6 (br s, Si*Me*$_3$), 16.4 (d, $^3J_{CP}$ = 5.6 Hz, *C*H$_3$), 63.7 (d, $^2J_{CP}$ = 6.9 Hz, *C*H$_2$), 126.7 (dt, ^1J = 271.7, 165.0 Hz, *C*F$_2$); ^{19}F NMR: δ −131.2 (d, $^2J_{FP}$ = 92.2 Hz); ^{31}P NMR: δ 9.65 (t, $^2J_{PF}$ = 92.2 Hz); GC–MS (EI) *m/z* 29 (12%), 45 (15), 65 (35), 73 (80), 81 (33), 93 (20), 121 (70), 141 (100), 153 (20), 165 (75), 205 (50), 233 (50), 259 [M]$^+$ (1).

4.2. Preparation of phosphonates 3

4.2.1. Diethyl 1,1-difluoro-2-phenyl-2-(trimethylsilyloxy)ethylphosphonate (3a) [16]

TBAT (22 mg, 0.04 mmol) was added to a solution of **1** (1.04 g, 4 mmol) and benzaldehyde (425 g, 4 mmol) in THF (4 mL). After 5 h of stirring, brine (3 mL) was added and the product was extracted into petrol ether (3 × 30 mL). The combined organic extract was dried ($MgSO_4$), filtered, concentrated under reduced pressure. After removal of impurities under vacuum (50 °C, 0.1 torr, 3 h) pure product was obtained as a colorless liquid (1.875 g, 94%): ^{1}H NMR: δ 0.07 (s, 9H, Si*Me*$_3$), 1.26 (t, 3H, $^3J_{HH}$ = 7.1 Hz, C*H*$_3$), 1.37 (t, 3H, $^3J_{HH}$ = 7.1 Hz, C*H*$_3$), 4.04–4.31 (m, 4H, 2 × C*H*$_2$), 5.08–5.14 (m, 1H, C*H*O), 7.33–7.36 (m, 3H, C$_{Ar}$*H*), 7.43–7.46 (m, 2H, C$_{Ar}$*H*); ^{13}C NMR: δ −0.1 (Si*Me*$_3$), 16.1–16.3 (m, *C*H$_3$), 64.1–64.3 (m, *C*H$_2$), 74.1–74.7 (m, *C*HO), 118.3 (ddd, ^1J = 273.0, 262.6, 208.1 Hz, *C*F$_2$), 127.8, 128.5, 128.6, 135.8–135.9 (m); ^{19}F NMR: δ −124.5 (ddd, 1F, $^2J_{FF}$ = 304.6 Hz, $^2J_{FP}$ = 104.4 Hz, $^3J_{FH}$ = 18.9 Hz),–115.6 (ddd, 1F, $^2J_{FF}$ = 304.6 Hz, $^2J_{FP}$ = 102.1 Hz, $^3J_{FH}$ = 7.3 Hz); ^{31}P NMR: δ 6.47 (dd, $^2J_{PF}$ = 104.4, 102.1 Hz); FTIR (film, ν_{max} cm^{-1}) 2983 (w), 1455 (w), 1268 (m), 1253 (m), 1182 (m), 1016 (s), 842 (s), 752 (m); GC–MS (EI) *m/z* 73 (30%), 155 (20), 179 (100), 180 (15), 233 (10), 260 (40), 351 [M–Me]$^+$ (5); HRMS (ESI$^+$) calculated for $C_{15}H_{26}F_2O_4PSi$: 367.13006, found: 367.12940.

4.2.2. Diethyl 1,1-difluoro-2-n-hexyl-2-(trimethylsilyloxy)ethylphosphonate (3e)

Solution of TBAT (20 mg, 37 μmol) in DMF (1.5 mL) was added dropwise to a solution of **1** (966 mg, 3.71 mmol) and *n*-heptanal (466 mg, 4.08 mmol) in DMF (2.5 mL) at −50 °C. The mixture was warmed up to rt, after 4 h of stirring, brine (3 mL) was added and the product was extracted into petrol ether (3 × 30 mL). The combined organic extract was dried ($MgSO_4$), filtered, concentrated under reduced pressure. After removal of impurities under vacuum (50 °C, 0.1 torr, 3 h) pure product was obtained as a colorless liquid (1.298 g, 93%): ^{1}H NMR: δ 0.16 (s, 9H, Si*Me*$_3$), 0.87–0.90 (m, 3H, C*H*$_3$(CH$_2$)$_5$), 1.24–1.34 (m, 7H, CH$_3$(C*H*$_2$)$_3$CH$_2$C*H*$_a$H$_b$), 1.36–1.40 (m, 6H, 2 × C*H*$_3$CH$_2$O), 1.41–1.58 (m, 1H, CH$_3$(CH$_2$)$_4$CH$_a$*H*$_b$), 1.65–1.80 (m, 2H, C*H*$_2$), 3.93–4.04 (m, 1H, C*H*O), 4.20–4.34 (m, 4H, 2 × C*H*$_2$O); ^{13}C NMR: δ 0.2 (Si*Me*$_3$), 14.0 (*C*H$_3$(CH$_2$)$_5$), 16.3 (d, $^3J_{CP}$ = 5.7 Hz, *C*H$_3$CH$_2$O), 22.6 (*C*H$_2$), 25.6 (*C*H$_2$), 29.0 (*C*H$_2$), 30.8 (*C*H$_2$), 31.7 (*C*H$_2$), 64.2–64.4 (m, *C*H$_2$O), 73.0–73.7 (m, *C*HO), 116.0–123.3 (m, *C*F$_2$); ^{19}F NMR: δ–119.5 (ddd, 1F, $^2J_{FF}$ = 303.8 Hz, $^2J_{FP}$ = 103.8 Hz, $^3J_{FH}$ = 16.0 Hz),–116.8 (ddd, 1F, $^2J_{FF}$ = 303.8 Hz, $^2J_{FP}$ = 105.2 Hz, $^3J_{FH}$ = 9.3 Hz); ^{31}P NMR: δ 6.63 (dd, $^2J_{PF}$ = 105.2, 103.8 Hz); FTIR (film, ν_{max} cm^{-1}) 1273 (s), 1253 (s), 1164 (m), 1025 (s), 845 (s), 754 (m); GC–MS (EI) *m/z* 55 (15%), 73 (40), 103 (15), 165 (20), 187 (75), 233 (50), 260 (100), 303 (25), 359 (35), 374 [M]$^+$ (1); HRMS (ESI$^+$) calculated for $C_{15}H_{34}F_2O_4PSi$: 375.1927, found: 375.1926.

4.2.3. Diethyl 1,1-difluoro-2-methyl-2-(trimethylsilyloxy)propylphosphonate (3f)

Solution of TBAT (25 mg, 47 μmol) in DMF (1 mL) was added dropwise to a solution of **1** (1.227 g, 4.70 mmol) and acetone (330 mg, 5.70 mmol) in DMF (2 mL) at −50 °C. The mixture was warmed up to rt, after 3 h of stirring brine (3 mL) was added and the product was extracted into petrol ether (3 × 30 mL). The combined organic extract was dried ($MgSO_4$), filtered and concentrated under reduced pressure. After removal of impurities under vacuum (50 °C, 0.1 torr, 3 h) pure product was obtained as a colorless liquid (1.265 g, 85%): ^{1}H NMR: δ 0.17 (s, 9H, Si*Me*$_3$), 1.37 (dt, 6H, $^3J_{HH}$ = 7.1 Hz, $^4J_{HP}$ = 0.5 Hz, 2 × C*H*$_3$CH$_2$), 1.45–1.46 (m, 6H, 2 × C*H*$_3$), 4.20–4.33 (m, 4H, 2 × C*H*$_2$); ^{13}C NMR: δ 2.2 (Si*Me*$_3$), 16.3 (d, $^3J_{CP}$ = 5.8 Hz, *C*H$_3$CH$_2$), 24.3–24.4 (m, *C*H$_3$), 63.6–64.3 (m, *C*H$_2$), 76.2 (dt, $^2J_{CF}$ = 23.3 Hz, $^2J_{CP}$ = 14.3 Hz, *C*CF$_2$), 107.7–136.1 (m, *C*F$_2$); ^{19}F NMR: δ −118.5 (d, $^2J_{FP}$ = 105.7 Hz); ^{31}P NMR: δ 6.77 (t, $^2J_{PF}$ = 105.7 Hz); FTIR (film, ν_{max} cm^{-1}) 2987 (m), 1389 (w), 1252 (m), 1199 (m), 1125 (m), 1064 (s), 1017 (s), 975 (m), 890 (m), 839 (s), 753 (m), 562 (m); GC–MS (EI) *m/z* 73 (75%), 131 (100), 155 (30), 260 (30); HRMS (ESI$^+$) calculated for $C_{11}H_{26}F_2O_4PSi$: 319.1301, found: 319.1306.

4.3. Preparation of "unsymmetrical" phosphates (5)

4.3.1. 1-Phenyl-2,2-difluoro-3-hydroxy-3-(4-chlorophenyl)propyl diethyl phosphate (5ab)

Solution of TBAT (11 mg, 21 μmol) in DMF (0.5 mL) was added to a solution of **1** (535 mg, 2.06 mmol) and benzaldehyde (218 mg, 2.06 mmol) in DMF (3 mL) at 0 °C. The mixture was warmed up to rt, after 4 h of stirring it was added dropwise to a mixture of TBAF (333 mg, 0.62 mmol) and 4-chlorobenzaldehyde (578 mg, 4.11 mmol) in DMF (3 mL). After 3 h of stirring three drops of distilled water were added and the mixture was stirred for further 2 h. Saturated NH_4Cl (3 mL) was added and the product was extracted into ethyl acetate (3 × 30 mL). The combined organic extract was washed with brine (10 mL), dried ($MgSO_4$), filtered, concentrated under reduced pressure, and purified on silica gel to yield separately *anti* and *syn* products. *Anti*-**5ab** (mixture of isomeric phosphates 61:39): pale yellow oil (378 mg, 42%): R_f (30% EtOAc/petrol ether) 0.29; ^{1}H NMR: δ 1.30 (dt, 3H, $^3J_{HH}$ = 7.1 Hz, $^4J_{HP}$ = 1.1 Hz, C*H*$_{3major}$), 1.30 (dt, 3H, $^3J_{HH}$ = 7.1 Hz, $^4J_{HP}$ = 1.0 Hz, C*H*$_{3minor}$), 1.34–1.38 (m, 3H + 3H, C*H*$_{3major+minor}$), 3.78–3.99 (m, 4H, 2 × C*H*$_{2minor}$), 4.13–4.28 (m, 4H, 2 × C*H*$_{2major}$), 5.14–5.21 (m, 1H + 1H, C*H*OH$_{major+minor}$), 5.35–5.41 (m, 1H, O*H*$_{minor}$), 5.60 (br s, 1H, O*H*$_{major}$), 5.73–5.82 (m, 1H + 1H, C*H*OP$_{major+minor}$), 7.30–7.48 (m, 9H + 9H, C$_{Ar}$*H*$_{major+minor}$); ^{13}C NMR: δ 15.7 (d, $^3J_{CP}$ = 6.7 Hz, *C*H$_3$), 15.8 (d, $^3J_{CP}$ = 7.1 Hz, *C*H$_3$), 16.0–16.1 (m, *C*H$_3$), 64.9 (d, $^2J_{CP}$ = 6.3 Hz, *C*H$_2$), 65.0 (d, $^2J_{CP}$ = 6.4 Hz, *C*H$_2$), 65.1 (d, $^2J_{CP}$ = 6.1 Hz, *C*H$_2$), 65.1 (d, $^2J_{CP}$ = 6.1 Hz, *C*H$_2$), 70.3 (dd, $^2J_{CF}$ = 29.9, 25.4 Hz, *C*HOH), 70.9 (dd, $^2J_{CF}$ = 29.6, 25.4 Hz, *C*HOH), 74.8–75.7 (m, *C*HOP), 119.2 (dt, $^1J_{CF}$ = 252.8 Hz, $^3J_{CP}$ = 7.5 Hz, *C*F$_2$), 127.9, 128.1, 128.2, 128.4, 128.5, 129.4, 129.5, 129.8, 131.4 (d, $^3J_{CP}$ = 2.9 Hz, C$_{Ar}$CHOP), 132.5 (d, $^3J_{CP}$ = 2.9 Hz, C$_{Ar}$CHOP), 134.1, 134.5, 135.4, 135.7; ^{19}F NMR: δ −122.3 to −122.2 (m); ^{31}P NMR: δ 0.26 (s$_{minor}$), 0.39 (s$_{major}$); GC–MS (EI) *m/z* 77 (10%), 99 (8), 140 (100), 155 (10), 173 (65), 274 (9); FTIR (film, ν_{max} cm^{-1}) 3329 (m), 3092 (w), 3067 (w), 3035 (w), 2986 (m), 1598 (w), 1493 (m), 1256 (m), 1164 (m), 1036 (s); HRMS (ESI$^+$) calculated for $C_{19}H_{22}ClF_2NaO_5P$: 457.0752, found: 457.0754. *Syn*-**5ab** (mixture of isomeric phosphates 69:31): white gummy solid (373 mg, 42%): R_f (30% EtOAc/petrol ether) 0.14; ^{1}H NMR: δ 1.03 (dt, 3H, $^3J_{HH}$ = 7.1 Hz, $^4J_{HP}$ = 1.1 Hz, C*H*$_{3major}$), 1.08 (dt, 3H, $^3J_{HH}$ = 7.1 Hz, $^4J_{HP}$ = 1.0 Hz, C*H*$_{3minor}$), 1.23 (dt, 3H,

$^3J_{HH}$ = 7.1 Hz, $^4J_{HP}$ = 1.1 Hz, CH_{3major}), 1.24 (dt, 3H, $^3J_{HH}$ = 7.1 Hz, $^4J_{HP}$ = 1.1 Hz, CH_{3minor}), 3.67–3.80 (m, 2H + 2H, 2 × C$H_{2major+minor}$), 3.96–4.09 (m, 2H + 2H, 2 × C$H_{2major+minor}$), 4.42–4.49 (m, 1H + 1H, CHO$H_{major+minor}$), 4.72 (d, $^3J_{HH}$ = 5.0 Hz, OH_{minor}), 4.96 (d, $^3J_{HH}$ = 5.1 Hz, OH_{major}), 5.93–6.03 (m, 1H + 1H, CHO$P_{major+minor}$), 7.25–7.31 (m, $C_{Ar}H$), 7.34–7.42 (m, $C_{Ar}H$), 7.58–7.64 (m, $C_{Ar}H$); ^{13}C NMR: δ 15.7 (d, $^3J_{CP}$ = 7.3 Hz, CH_3), 15.9 (d, $^3J_{CP}$ = 7.1 Hz, CH_3), 63.9 (d, $^2J_{CP}$ = 6.0 Hz, CH_2), 64.4 (d, $^2J_{CP}$ = 6.1 Hz, CH_2), 71.8 (dd, $^2J_{CF}$ = 30.4, 23.6 Hz, CHOH), 72.4 (dd, $^2J_{CF}$ = 29.8, 24.2 Hz, CHOH), 77.6–78.2 (m, CHOP), 117.1–122.2 (m, CF_2), 128.0, 128.1, 128.15, 128.5, 128.6, 128.7, 128.8, 129.5, 130.1, 132.4–132.5 (m), 133.7–133.8 (m), 134.4, 135.0, 135.5, 136.2; ^{19}F NMR: δ −123.9 (ddd, 1F$_{major}$, $^2J_{FF}$ = 251.1 Hz, $^3J_{FH}$ = 19.3, 6.5 Hz),–122.7 (dd, 1F$_{major}$, $^2J_{FF}$ = 251.1 Hz, $^3J_{FH}$ = 17.3 Hz),–123.8 (ddd, 1F$_{minor}$, $^2J_{FF}$ = 251.1 Hz, $^3J_{FH}$ = 18.1, 7.9 Hz),–123.0 (dd, 1F$_{minor}$, $^2J_{FF}$ = 250.6 Hz, $^3J_{FH}$ = 15.4 Hz); ^{31}P NMR: δ −1.02 (s$_{minor}$),–0.98 (s$_{major}$); GC–MS (EI) *m/z* 77 (15%), 99 (10), 140 (100), 155 (25), 174 (75); FTIR (film, ν_{max} cm^{-1}) 3312 (m), 3067 (w), 3037 (w), 2985 (w), 1599 (w), 1493 (m), 1254 (m), 1162 (m), 1025 (s); HRMS (ESI$^+$) calculated for $C_{19}H_{22}ClF_2NaO_5P$: 457.0752, found: 457.0754.

4.3.2. 1-Phenyl-2,2-difluoro-3-hydroxy-3-(4-methylphenyl)propyl diethyl phosphate (**5ac**)

Solution of TBAT (8 mg, 15 μmol) in DMF (0.5 mL) was added to a solution of **1** (405 mg, 1.56 mmol) and benzaldehyde (165 mg, 1.56 mmol) in DMF (3 mL) at 0 °C. The mixture was warmed up to rt, after 4 h of stirring it was added dropwise to a mixture of CsF (118 mg, 0.78 mmol) and 4-methylbenzaldehyde (374 mg, 3.12 mmol) in DMF (2.5 mL). After additional 1 h of stirring three drops of distilled water were added and the mixture was stirred for further 2 h. Saturated NH_4Cl (3 mL) was added and the product was extracted into ethyl acetate (3 × 30 mL). The combined organic extract was washed with brine (10 mL), dried ($MgSO_4$), filtered, concentrated under reduced pressure, and purified on silica gel to yield separately *anti* and *syn* products. *Anti*-**5ac** (mixture of isomeric phosphates 50:50): colorless oil (239 mg, 37%): R_f (30% EtOAc/petrol ether) 0.24; ^{1}H NMR: δ 1.06–1.12 (m, 6H, 2 × CH_3CH$_2$), 1.35 (dt, 3H, $^3J_{HH}$ = 7.1 Hz, $^4J_{HP}$ = 1.0 Hz, CH_3CH$_2$), 1.36 (dt, 3H, $^3J_{HH}$ = 7.1 Hz, $^4J_{HP}$ = 1.0 Hz, CH_3CH$_2$), 2.32 (s, 3H, $C_{Ar}CH_3$), 2.33 (s, 3H, $C_{Ar}CH_3$), 3.81–3.87 (m, 2H, CH_2), 3.89–3.97 (m, 2H, CH_2), 4.10–4.27 (m, 4H, 2 × CH_2), 5.10–5.18 (m, 2H, 2 × CHOH), 5.22 (d, 1H, $^3J_{HH}$ = 5.6 Hz, OH), 5.35 (d, 1H, $^3J_{HH}$ = 5.3 Hz, OH), 5.71–5.82 (m, 2H, 2 × CHOP), 7.13–7.17 (m, $C_{Ar}H$), 7.29–7.39 (m, $C_{Ar}H$), 7.44–7.49 (m, $C_{Ar}H$); ^{13}C NMR: δ 15.7 (d, $^3J_{CP}$ = 6.7 Hz, CH_3CH_2), 15.8 (d, $^3J_{CP}$ = 6.6 Hz, CH_3CH_2), 16.0 (d, $^3J_{CP}$ = 6.7 Hz, CH_3CH_2), 21.1 (s, $C_{Ar}CH_3$), 21.2 (s, $C_{Ar}CH_3$), 64.8 (d, $^2J_{CP}$ = 6.3 Hz, CH_2), 64.9 (d, $^2J_{CP}$ = 6.3 Hz, CH_2), 65.0 (d, $^2J_{CP}$ = 6.1 Hz, CH_2), 70.6–71.2 (m, CHOH), 75.1–75.9 (m, CHOP), 119.3 (dt, $^1J_{CF}$ = 252.9 Hz, $^3J_{CP}$ = 7.6 Hz, CF_2), 127.9, 127.9, 128.0, 128.1, 128.2, 128.3, 128.4, 128.7, 129.3, 129.7 (d, $^3J_{CP}$ = 3.0 Hz), 132.7–132.8 (m), 135.8, 138.0, 139.2; ^{19}F NMR: δ −122.4 to −122.2 (m); ^{31}P NMR: δ 0.45 (s), 0.58 (s); GC–MS (EI) *m/z* 77 (10%), 91 (10), 119 (12), 140 (100), 154 (80); FTIR (film, ν_{max} cm^{-1}) 3345 (m), 3092 (w), 3065 (w), 3034 (w), 2986 (m), 1617 (w), 1516 (w), 1496 (w), 1255 (m), 1164 (m), 1029 (s); HRMS (ESI$^+$) calculated for $C_{20}H_{25}F_2NaO_5P$: 437.1300, found: 437.1302. *Syn*-**5ac** (mixture of isomeric phosphates 53:47): colorless oil (232 mg, 36%): R_f (30% EtOAc/petrol ether) 0.09; ^{1}H NMR: δ 1.02–1.07 (m, 6H, CH_3CH$_{2major+minor}$), 1.21–1.24 (m, 6H, CH_3CH$_{2major+minor}$), 2.31 (s, 3H, $C_{Ar}CH_{3minor}$), 2.73 (s, 3H, $C_{Ar}CH_{3major}$), 3.68–3.81 (m, 4H, 2 × CH_{2minor}), 3.97–4.10 (m, 4H, 2 × CH_{2major}), 4.19–4.23 (m, 2H, O$H_{major+minor}$), 4.43–4.53 (m, 2H, CHO$H_{major+minor}$), 5.91–6.02 (m, 2H, CHO$P_{major+minor}$), 7.10 (d, 2H, $^3J_{HH}$ = 8.0 Hz, $C_{Ar}H_{minor}$), 7.20 (d, 2H, $^3J_{HH}$ = 8.1 Hz, $C_{Ar}H_{major}$), 7.23 (d, 2H, $^3J_{HH}$ = 8.1 Hz, $C_{Ar}H_{major}$), 7.27–7.29 (m, $C_{Ar}H$), 7.34–7.36 (m, $C_{Ar}H$), 7.39–7.40 (m, $C_{Ar}H$), 7.50–7.53 (m, $C_{Ar}H$); ^{13}C NMR: δ 15.6 (d, $^3J_{CP}$ = 7.1 Hz, CH_3CH_2), 15.7 (d, $^3J_{CP}$ = 7.1 Hz, CH_3CH_2), 15.8 (d, $^3J_{CP}$ = 7.1 Hz, CH_3CH_2), 21.1 (s, $C_{Ar}CH_3$), 21.2 (s, $C_{Ar}CH_3$), 63.7 (d, $^2J_{CP}$ = 5.8 Hz, CH_2), 64.1 (d, $^2J_{CP}$ = 5.7 Hz, CH_2), 64.2 (d, $^2J_{CP}$ = 5.6 Hz, CH_2), 72.0–72.7 (m, CHOH), 77.6–78.2 (m, CHOP), 117.1–122.3 (m, CF_2), 127.8, 127.9, 128.0, 128.4, 128.5, 128.6, 128.7, 129.1, 129.3, 130.8, 130.8–130.9 (m), 132.4, 133.2, 133.9–134.0 (m), 136.3, 138.2, 139.2; ^{19}F NMR: δ −124.0 (ddd, 1F$_{minor}$, $^2J_{FF}$ = 250.4 Hz, $^3J_{FH}$ = 19.4, 6.9 Hz),–122.7 (dd, 1F$_{minor}$, $^2J_{FF}$ = 250.4 Hz, $^3J_{FH}$ = 16.8 Hz),–123.9 (ddd, 1F$_{major}$, $^2J_{FF}$ = 250.7 Hz, $^3J_{FH}$ = 19.5, 6.9 Hz),–122.6 (dd, 1F$_{major}$, $^2J_{FF}$ = 250.7 Hz, $^3J_{FH}$ = 17.3 Hz); ^{31}P NMR: δ −0.95 (s$_{minor}$),–0.93 (s$_{major}$); GC–MS (EI) *m/z* 77 (10%), 91 (10), 119 (12), 140 (100), 154 (60); FTIR (film, ν_{max} cm^{-1}) 3330 (m), 3091 (w), 3065 (w), 3034 (m), 2983 (m), 1614 (w), 1580 (w), 1516 (m), 1263 (s), 1162 (s), 1030 (s); HRMS (ESI$^+$) calculated for $C_{20}H_{25}F_2NaO_5P$: 437.1300, found: 437.1303.

4.3.3. 1-(4-Chlorophenyl)-2,2-difluoro-3-hydroxy-3-(4-methoxyphenyl)propyl diethyl phosphate (**5bd**)

Solution of TBAT (10 mg, 19 μmol) in DMF (0.5 mL) was added to a solution of **1** (484 mg, 1.86 mmol) and 4-chlorobenzaldehyde (261 mg, 1.86 mmol) in DMF (3 mL) at 0 °C. The mixture was warmed up to rt, after 4 h of stirring it was added dropwise to a mixture of CsF (141 mg, 0.93 mmol) and 4-methoxybenzaldehyde (506 mg, 3.72 mmol) in DMF (2.5 mL). After additional 1.5 h of stirring three drops of distilled water were added and the mixture was stirred for further 2 h. Saturated NH_4Cl (4 mL) was added and the product was extracted into ethyl acetate (3 × 30 mL). The combined organic extract was washed with brine (10 mL), dried ($MgSO_4$), filtered, concentrated under reduced pressure, and purified on silica gel to yield separately *anti* and *syn* products. *Anti*-**5bd** (mixture of isomeric phosphates 67:33): colorless oil (296 mg, 34%): R_f (30% EtOAc/petrol ether) 0.14; ^{1}H NMR: δ 1.09–1.16 (m, 6H, CH_3CH$_{2major+minor}$), 1.35–1.39 (m, 6H, CH_3CH$_{2major+minor}$), 3.77 (s, 3H, OCH_{3minor}), 3.78 (s, 3H, OCH_{3major}), 3.80–3.97 (m, 4H, 2 × CH_{2minor}), 4.13–4.25 (m, 4H, 2 × CH_{2major}), 5.08–5.21 (m, 3H, CHO$H_{major+minor}$ + OH_{minor}), 5.55 (d, 1H, $^3J_{HH}$ = 4.9 Hz, OH_{major}), 5.68–5.80 (m, 2H, CHO$P_{major+minor}$), 6.86–6.90 (m, $C_{Ar}H$), 7.30–7.43 (m, $C_{Ar}H$); ^{13}C NMR: δ 15.7 (d, $^3J_{CP}$ = 6.7 Hz, CH_3CH_2), 15.8 (d, $^3J_{CP}$ = 6.4 Hz, CH_3CH_2), 15.9 (d, $^3J_{CP}$ = 6.7 Hz, CH_3CH_2), 55.1 (s, OCH_3), 55.2 (s, OCH_3), 64.8–65.0 (m, CH_2), 70.0–70.7 (m, CHOH), 74.5–75.4 (m, CHOP), 116.5–121.6 (m, CF_2), 124.4 (d, $^3J_{CP}$ = 3.1 Hz), 127.9, 128.4, 128.7, 129.1, 129.3, 129.7, 130.8, 131.3 (d, $^3J_{CP}$ = 2.9 Hz), 132.4, 134.0, 134.4, 135.3, 159.6, 160.4, 167.7; ^{19}F NMR: δ −122.5 to −122.2 (m); ^{31}P NMR: δ 0.35 (s$_{minor}$), 0.59 (s$_{major}$); FTIR (film, ν_{max} cm^{-1}) 3329 (m), 3072 (w), 3038 (w), 2983 (m), 2840 (w), 1614 (m), 1587 (w), 1516 (m), 1253 (s), 1164 (m), 1033 (s); HRMS (ESI$^+$) calculated for $C_{20}H_{24}ClF_2NaO_6P$: 487.0859, found: 487.0860. *Syn*-**5bd** (mixture of isomeric phosphates 71:29): colorless oil (297 mg, 34%): R_f (30% EtOAc/petrol ether) 0.06; ^{1}H NMR: δ 1.03–1.09 (m, 6H, CH_3CH$_{2major+minor}$), 1.21–1.26 (m, 6H, CH_3CH$_{2major+minor}$), 3.70 (s, 3H, OCH_{3minor}), 3.84 (s, 3H, OCH_{3major}), 3.96–4.07 (m, 4H, C$H_{2major+minor}$), 4.17–4.25 (m, 4H, C$H_{2major+minor}$), 4.36–4.47 (m, 2H, CHO$H_{major+minor}$), 5.01–5.34 (br s, O$H_{major+minor}$), 5.91–6.00 (m, 2H, CHO$P_{major+minor}$), 6.82 (d, 1H, $^3J_{HH}$ = 8.8 Hz, $C_{Ar}H$), 6.91–6.94 (m, $C_{Ar}H$), 7.24–7.31 (m, $C_{Ar}H$), 7.37–7.40 (m, $C_{Ar}H$), 7.50–7.59 (m, $C_{Ar}H$), 7.68–7.70 (m, $C_{Ar}H$); ^{13}C NMR: δ 15.6 (d, $^3J_{CP}$ = 7.1 Hz, CH_3CH_2), 15.7 (d, $^3J_{CP}$ = 7.0 Hz, CH_3CH_2), 55.0 (s, OCH_3), 55.1 (s, OCH_3), 63.7 (d, $^2J_{CP}$ = 5.9 Hz, CH_2), 63.8 (d, $^2J_{CP}$ = 5.9 Hz, CH_2), 64.1 (d, $^2J_{CP}$ = 5.9 Hz, CH_2), 64.2 (d, $^2J_{CP}$ = 6.0 Hz, CH_2), 71.3–72.1 (m, CHOH), 77.2–77.8 (m, CHOP), 117.0–122.3 (m, CF_2), 125.7 (d, $^3J_{CP}$ = 3.1 Hz), 127.9, 128.5, 128.6, 129.2, 129.4, 129.9, 130.8, 132.3, 132.4 (d, $^3J_{CP}$ = 2.9 Hz), 134.1, 135.1, 135.3, 159.7, 160.3, 167.6; ^{19}F NMR: δ −123.9 (ddd, 1F$_{major}$, $^2J_{FF}$ = 250.5 Hz, $^3J_{FH}$ = 17.7, 8.0 Hz),–123.1 (dd, 1F$_{major}$, $^2J_{FF}$ = 250.5 Hz, $^3J_{FH}$ = 16.0 Hz),–124.1 (ddd, 1F$_{minor}$, $^2J_{FF}$ = 249.8 Hz, $^3J_{FH}$ = 17.7, 7.6 Hz),–123.2 (dd, 1F$_{minor}$, $^2J_{FF}$ = 249.8 Hz, $^3J_{FH}$ = 15.2 Hz); ^{31}P NMR: δ −1.00 (s$_{minor}$),–0.92 (s$_{major}$); FTIR (film,

ν_{max} cm^{-1}) 3320 (m), 3071 (w), 1614 (m), 1585 (m), 1515 (s), 1253 (s), 1163 (m), 1031 (s); HRMS (ESI$^+$) calculated for $C_{20}H_{24}ClF_2NaO_6P$: 487.0859, found: 487.0859.

4.3.4. 1-n-Hexyl-2,2-difluoro-3-hydroxy-3-phenylpropyl diethyl phosphate (**5ea**)

Solution of phosphonate **3e** (527.9 mg, 1.41 mmol) in DMF (2 mL) was added dropwise to a mixture of benzaldehyde (299 mg, 2.82 mmol) and CsF (107 mg, 0.71 mmol) in DMF (1.5 mL) at rt. After additional 3 h of stirring three drops of distilled water were added and the mixture was stirred for 1 h. Saturated NH_4Cl (4 mL) was added and the product was extracted into ethyl acetate (3 × 30 mL). The combined organic extract was washed with brine (10 mL), dried ($MgSO_4$), filtered, concentrated under reduced pressure, and purified on silica gel to yield separately *anti* and *syn* products. *Anti*-**5ea**: colorless oil (179 mg, 31%): R_f (30% EtOAc/petrol ether) 0.19; ^{1}H NMR: δ 0.86–0.90 (m, 4H, *n*-C_6H_{13}), 1.08 (dt, 3H, $^3J_{HH}$ = 7.0 Hz, $^4J_{HP}$ = 0.8 Hz, CH_3CH_2O), 1.26–1.41 (m, 14H, *n*-C_6H_{13}, CH_3CH_2O), 1.61–1.67 (m, 2H, *n*-C_6H_{13}), 3.76–3.86 (m, 1H, CH_aH_bO), 3.88–3.97 (m, 1H, CH_aH_bO), 3.98–4.08 (m, 1H, CHOH), 4.10–4.25 (m, 2H, CH_2O), 4.70 (d, 1H, $^3J_{HH}$ = 5.8 Hz, OH), 5.61–5.70 (m, 1H, CHOP), 7.38–7.41 (m, 3H, $C_{Ar}H$), 7.42–7.47 (m, 2H, $C_{Ar}H$); ^{13}C NMR: δ 14.0, 15.7 (d, $^3J_{CP}$ = 6.7 Hz, CH_3CH_2O), 16.0 (d, $^3J_{CP}$ = 6.6 Hz, CH_3CH_2O), 22.6, 25.7, 28.0–28.1 (m), 29.1, 31.7, 64.8 (d, $^2J_{CP}$ = 6.5 Hz, OCH_2), 64.9 (d, $^2J_{CP}$ = 6.1 Hz, OCH_2), 69.0 (dd, $^2J_{CF}$ = 29.5, 26.8 Hz, CHOH), 75.0 (ddd, $^2J_{CF}$ = 34.9, 29.2 Hz, $^2J_{CP}$ = 4.6 Hz, CHOP), 120.2 (ddd, $^1J_{CF}$ = 254.3, 252.6 Hz, $^3J_{CP}$ = 6.9 Hz, CF_2), 128.2, 128.3, 129.2, 132.8 (d, $^3J_{CP}$ = 3.2 Hz); ^{19}F NMR: δ −125.4 to −125.3 (m); ^{31}P NMR: δ 0.53 (s); FTIR (film, ν_{max} cm^{-1}) 3377 (m), 3094 (w), 3068 (w), 3037 (w), 2983 (m), 1498 (w), 1259 (s), 1167 (m), 1037 (s); GC–MS (EI) *m/z* 91 (10%), 99 (15), 107 (20), 127 (10), 140 (100), 155 (35), 243 (18), 274 (10); HRMS (ESI$^+$) calculated for $C_{19}H_{31}F_2NaO_5P$: 431.1769, found: 431.1769. *Syn*-**5ea**: colorless oil (187 mg, 33%): R_f (30% EtOAc/petrol ether) 0.40; ^{1}H NMR: δ 0.87–0.91 (m, 4H, *n*-C_6H_{13}), 1.30–1.43 (m, 13H, *n*-C_6H_{13}, CH_3CH_2O), 1.76–1.82 (m, 2H, *n*-C_6H_{13}), 4.17–4.27 (m, 4H, 2 × CH_2O), 4.74–4.85 (m, 1H, CHOH), 5.00–5.07 (m, 1H, CHOP), 5.58–5.59 (br s, 1H, OH), 7.32–7.38 (m, 3H, $C_{Ar}H$), 7.46–7.48 (m, 2H, $C_{Ar}H$); ^{13}C NMR: 14.0, 16.0–16.2 (m, CH_3CH_2O), 22.6, 25.0, 28.1–28.2, 29.1, 31.7, 64.9 (d, $^2J_{CP}$ = 6.1 Hz, OCH_2), 65.0 (d, $^2J_{CP}$ = 5.7 Hz, OCH_2), 70.4 (dd, $^2J_{CF}$ = 31.0, 24.5 Hz, CHOH), 75.2 (ddd, $^2J_{CF}$ = 37.1, 27.7 Hz, $^2J_{CP}$ = 5.9 Hz, CHOP), 120.1 (dt, $^1J_{CF}$ = 252.7 Hz, $^3J_{CP}$ = 4.8 Hz, CF_2), 127.9, 128.1–128.2 (m), 135.9–136.0 (m); ^{19}F NMR: δ −124.4 (dd, 1F, $^2J_{FF}$ = 263.6 Hz, $^3J_{FH}$ = 19.5 Hz),–123.4 (ddd, 1F, $^2J_{FF}$ = 263.6 Hz, $^3J_{FH}$ = 17.3, 5.3 Hz); ^{31}P NMR: δ 0.93 (s); FTIR (film, ν_{max} cm^{-1}) 3343 (m), 3092 (w), 3066 (w), 3034 (w), 2983 (m), 1605 (w), 1496 (w), 1264 (s), 1032 (s); GC–MS (EI) *m/z* 99 (50%), 127 (33), 140 (25), 155 (100); HRMS (ESI$^+$) calculated for $C_{19}H_{31}F_2NaO_5P$: 431.1769, found: 431.1765.

4.3.5. 1-n-Hexyl-2,2-difluoro-3-hydroxy-3-(4-chlorophenyl)propyl diethyl phosphate (**5eb**)

Prepared in analogy to **5ea** starting from 4-chlorobenzaldehyde yielding separately *anti* and *syn* products in 1:1 ratio. *Anti*-**5eb** (mixture of isomeric phosphates 75:25): colorless oil (170 mg, 31%): R_f (30% EtOAc/petrol ether) 0.35, 0.50; ^{1}H NMR: δ 0.88–0.91 (m, 3H + 3H, *n*-$C_6H_{13major+minor}$), 1.30–1.42 (m, 13H +13H, $CH_3CH_2O_{major+minor}$, *n*-$C_6H_{13major+minor}$), 1.54–1.61 (m, 1H +1H, *n*-$C_6H_{13major+minor}$), 1.75–1.85 (m, 2H + 2H, *n*-$C_6H_{13major+minor}$), 3.76–3.86 (m, 1H + 1H, $CH_2O_{major+minor}$), 3.88–3.97 (m, 1H + 1H, $CH_2O_{major+minor}$), 3.98–4.08 (m, 1H, $CHOH_{major}$), 4.10–4.25 (m, 4H, $CH_2O_{major+minor}$), 4.70 (d, 1H, $^3J_{HH}$ = 5.8 Hz, OH_{major}), 4.71–4.83 (m, 1H, $CHOH_{minor}$), 4.96–5.04 (m, 1H, $CHOP_{minor}$), 5.61–5.70 (m, 1H, $CHOP_{major}$), 5.96 (d, 1H, $^3J_{HH}$ = 3.3 Hz, OH_{minor}), 7.36–7.42 (m, 4H, $C_{Ar}H_{major+minor}$), 7.42–7.47 (m, 4H, $C_{Ar}H_{major+minor}$); ^{13}C NMR: δ 13.9, 14.0, 15.7 (d, $^3J_{CP}$ = 6.6 Hz, CH_3CH_2O), 15.9 (d, $^3J_{CP}$ = 6.9 Hz, CH_3CH_2O), 16.0 (d, $^3J_{CP}$ = 6.7 Hz, CH_3CH_2O), 16.1 (d, $^3J_{CP}$ = 6.9 Hz, CH_3CH_2O), 22.4, 22.5, 25.0, 25.6, 28.0–28.1 (m), 28.5–28.6 (m), 28.9, 29.1, 31.5, 31.7, 64.8 (d, $^2J_{CP}$ = 6.2 Hz, OCH_2), 64.9 (d, $^2J_{CP}$ = 6.2 Hz, OCH_2), 64.9 (d, $^2J_{CP}$ = 6.2 Hz, OCH_2), 65.0 (d, $^2J_{CP}$ = 5.7 Hz, OCH_2), 68.8 (dd, $^2J_{CF}$ = 29.7, 26.4 Hz, CHOH), 69.7 (dd, $^2J_{CF}$ = 31.0, 24.6 Hz, CHOH), 73.9–74.6 (m, CHOP), 74.9 (ddd, $^2J_{CF}$ = 36.9, 27.8 Hz, $^2J_{CP}$ = 5.8 Hz, CHOP), 117.5–122.6 (m, CF_2), 119.9 (dt, $^1J_{CF}$ = 252.9 Hz, $^3J_{CP}$ = 4.7 Hz, CF_2), 127.9, 128.4, 129.4, 129.6, 131.4 (d, $^3J_{CP}$ = 3.3 Hz), 133.9, 134.4 (d, $^3J_{CP}$ = 3.2 Hz), 135.3; ^{19}F NMR: δ −124.4 (dd, $1F_{major}$, $^2J_{FF}$ = 263.7 Hz, $^3J_{FH}$ = 19.3 Hz),–123.5 (ddd, $1F_{major}$, $^2J_{FF}$ = 263.9 Hz, $^3J_{FH}$ = 17.3, 5.3 Hz);–125.8 (ddd, $1F_{minor}$, $^2J_{FF}$ = 262.9 Hz, $^3J_{FH}$ = 16.9, 7.0 Hz),–125.0 (ddd, $1F_{minor}$, $^2J_{FF}$ = 263.0 Hz, $^3J_{FH}$ = 17.8, 5.9 Hz); ^{31}P NMR: δ 0.55 (s_{minor}), 0.99 (s_{major}); FTIR (film, ν_{max} cm^{-1}) 3330 (m), 3073 (w), 1598 (w), 1493 (m), 1251 (m), 1169 (m), 1032 (s); GC–MS (EI) *m/z* 99 (50%), 127 (40), 141 (10), 155 (100), 174 (15); HRMS (ESI$^+$) calculated for $C_{19}H_{30}ClF_2NaO_5P$: 465.1380, found: 465.1375. *Syn*-**5eb** (mixture of isomeric phosphates 80:20): white solid (170 mg, 31%): m.p. 77–78 °C, R_f (25% EtOAc/petrol ether) 0.26, 0.16; ^{1}H NMR: δ 0.84–0.91 (m, 3H +3H, *n*-$C_6H_{13major+minor}$), 1.09 (dt, 3H, $^3J_{HH}$ = 7.1 Hz, $^4J_{HP}$ = 0.7 Hz, $CH_3CH_2O_{minor}$), 1.24–1.32 (m, 7H + 7H *n*-$C_6H_{13major+minor}$, 6H $CH_3CH_2O_{major}$, 3H $CH_3CH_2O_{minor}$), 1.40–1.60 (m, 1H +1H, *n*-$C_6H_{13major+minor}$), 1.81–1.87 (m, 2H +2H, *n*-$C_6H_{13major+minor}$), 3.30–3.39 (m, 1H, $CHOH_{minor}$), 3.60 (d, 1H, $^3J_{HH}$ = 8.5 Hz, OH_{minor}), 3.75-3.84 (m, 2H, CH_2O_{minor}), 3.99–4.15 (m, 4H + 2H, $CH_2O_{major+minor}$), 4.79–4.95 (m, 2H, CHOH, $CHOP_{major}$), 5.01 (d, 1H, $^3J_{HH}$ = 5.5 Hz, OH_{major}), 5.77–5.86 (m, $CHOP_{minor}$), 7.31–7.33 (m, 2H, $C_{Ar}H_{major}$), 7.34–7.37 (m, 2H, $C_{Ar}H_{minor}$), 7.42 (d, 2H, $^3J_{HH}$ = 8.4 Hz, $C_{Ar}H_{major}$), 7.49 (d, 2H, $^3J_{HH}$ = 8.4 Hz, $C_{Ar}H_{minor}$); ^{13}C NMR: δ 14.0, 14.0, 15.8 (d, $^3J_{CP}$ = 7.0 Hz, CH_3CH_2O), 15.9–16.1 (m, CH_3CH_2O), 22.5, 22.6, 25.0, 25.3, 29.1, 29.2, 29.2–29.3 (m), 29.8–29.9 (m), 31.7, 64.0–64.1 (m), 64.2 (d, $^2J_{CP}$ = 6.1 Hz, OCH_2), 64.4 (d, $^2J_{CP}$ = 6.0 Hz, OCH_2), 70.6 (dd, $^2J_{CF}$ = 29.4, 24.9 Hz, CHOH), 72.2 (dd, $^2J_{CF}$ = 30.8, 24.3 Hz, CHOH), 77.3–77.9 (m, CHOP), 120.0 (ddd, $^1J_{CF}$ = 254.9, 248.7 Hz, $^3J_{CP}$ = 4.3 Hz, CF_2), 120.7 (ddd, $^1J_{CF}$ = 258.5, 252.3 Hz, $^3J_{CP}$ = 6.8 Hz, CF_2), 128.2, 128.7, 129.5, 129.9, 132.5 (dd, ^3J = 5.3, 2.2 Hz), 134.3, 135.3, 135.5; ^{19}F NMR: δ −126.1 (ddd, $1F_{minor}$, $^2J_{FF}$ = 249.9 Hz, $^3J_{FH}$ = 19.4, 6.7 Hz),–124.6 (dd, $1F_{minor}$, $^2J_{FF}$ = 250.4 Hz, $^3J_{FH}$ = 16.3 Hz), −121.1 (ddd, $1F_{major}$, $^2J_{FF}$ = 256.6 Hz, $^3J_{FH}$ = 19.1, 6.7 Hz),–118.2 (dd, $1F_{major}$, $^2J_{FF}$ = 256.6 Hz, $^3J_{FH}$ = 13.3 Hz); ^{31}P NMR: δ −1.03 (s_{major}),–0.83 (s_{minor}); FTIR (film, ν_{max} cm^{-1}) 3321 (m), 3073 (w), 1599 (w), 1580 (w), 1493 (m), 1253 (s), 1167 (m), 1036 (s); GC–MS (EI) *m/z* 99 (40%), 127 (45), 141 (30), 155 (100), 174 (40); HRMS (ESI$^+$) calculated for $C_{19}H_{30}ClF_2NaO_5P$: 465.1380, found: 465.1375.

4.3.6. 1,1-Dimethyl-2,2-difluoro-3-hydroxy-3-(4-chlorophenyl)propyl diethyl phosphate (**5fb**)

Prepared in analogy to **5ea** starting from **3f** and 4-chlorobenzaldehyde in 4 h reaction time yielding the product **5fb** (mixture of isomeric phosphates 67:33) as light yellow oil (566 mg, 56%): R_f (30% EtOAc/petrol ether) 0.20. The spectroscopic characterization data were identical to those published by us [5a].

4.4. Preparation of "symmetrical" phosphates (**5**)

4.4.1. 2,2-Difluoro-3-hydroxy-1,3-diphenylpropyl diethyl phosphate (**5aa**) [5a]

Solution of TBAT (324 mg, 0.60 mmol) in DMF (1.5 mL) was added dropwise to a solution of **1** (312 mg, 1.20 mmol) and benzaldehyde (509 mg, 4.80 mmol) in DMF (3 mL) at 0 °C. The mixture was warmed up to rt, after 5 h of stirring three drops of distilled water were added and the mixture was stirred for further 2 h. Saturated NH_4Cl (3 mL) was added and the product was extracted into ethyl acetate (3 × 30 mL). The combined organic extract was washed with brine (10 mL), dried ($MgSO_4$), filtered,

concentrated under reduced pressure, and purified on silica gel to yield separately *anti* and *syn* products in 1:1 ratio and total 89% yield. The spectroscopic characterization data were identical to those published by us [5a].

4.4.2. 1,3-Bis(4-chlorophenyl)-2,2-difluoro-3-hydroxypropyl diethyl phosphate (**5bb**) [5a]

Prepared in analogy to **5aa** in 2 h reaction time, yielding separately *anti* and *syn* products in 1:1 ratio and total 77% yield. The spectroscopic characterization data were identical to those published by us [5a].

4.4.3. 1,3-Bis(4-methylphenyl)-2,2-difluoro-3-hydroxypropyl diethyl phosphate (**5cc**)

Solution of **1** (364 mg, 1.40 mmol) and 4-methylbenzaldehyde (672 mg, 5.59 mmol) in DMF (2 mL) was added dropwise to a suspension of CsF (106 mg, 0.70 mmol) in DMF (2 mL), cooled to −5 °C. The mixture was warmed up to rt and after 2 h of stirring three drops of distilled water were added. After 2 h of stirring saturated NH_4Cl (7 mL) was added and the product was extracted into ethyl acetate (3 × 30 mL). The combined organic extract was washed with brine (10 mL), dried ($MgSO_4$), filtered, concentrated under reduced pressure, and purified on silica gel to yield separately *anti* and *syn* products in 1:1 ratio. *Anti*-**5cc**: white solid (838 mg, 42%): m.p. 94–95 °C, R_f (30% EtOAc/petrol ether) 0.20; ^{1}H NMR: δ 1.12 (dt, 3H, $^3J_{HH}$ = 7.1 Hz, $^4J_{HP}$ = 1.0 Hz, CH_3CH$_2$), 1.38 (dt, 3H, $^3J_{HH}$ = 7.1 Hz, $^4J_{HP}$ = 1.1 Hz, CH_3CH$_2$), 2.33 (s, 3H, C$_{Ar}$CH_3), 2.34 (s, 3H, C$_{Ar}$CH_3), 3.81–3.91 (m, 1H, CH_aH$_b$), 3.91–4.01 (m, 1H, CH$_a$$H_b$), 4.15–4.27 (m, 2H, C$H_2$), 5.08–5.17 (m, 2H, O*H*, C*H*OH), 5.69–5.78 (m, 1H, C*H*OP), 7.14–7.18 (m, 4H, C$_{Ar}$*H*), 7.33–7.37 (m, 4H, C$_{Ar}$*H*); ^{13}C NMR: δ 15.7 (d, $^3J_{CP}$ = 6.7 Hz, *C*H$_3$CH$_2$), 15.9 (d, $^3J_{CP}$ = 6.7 Hz, *C*H$_3$CH$_2$), 21.1 (s, C$_{Ar}$CH$_3$), 21.1 (s, C$_{Ar}$CH$_3$), 64.7 (d, $^2J_{CP}$ = 6.4 Hz, *C*H$_2$), 64.9 (d, $^2J_{CP}$ = 6.1 Hz, *C*H$_2$), 70.7 (dd, $^2J_{CF}$ = 29.5, 25.7 Hz, *C*HOH), 75.1–75.7 (m, *C*HOP), 119.2 (ddd, $^1J_{CF}$ = 260.1, 252.8 Hz, $^3J_{CP}$ = 7.4 Hz, *C*F$_2$), 127.9, 128.2, 128.6, 128.8, 129.7 (d, $^3J_{CP}$ = 3.0 Hz),132.7, 137.8, 139.1; ^{19}F NMR: δ −122.6 to −122.5 (m); ^{31}P NMR: δ 0.68 (s); GC–MS (EI) *m/z* 91 (40%), 119 (12), 154 (100); FTIR (film, ν_{max} cm^{-1}) 3341 (s), 3100 (w), 3030 (m), 2986 (m), 1617 (w), 1516 (m), 1254 (m), 1163 (m), 1033 (s); HRMS (ESI$^+$) calculated for $C_{21}H_{27}F_2NaO_5P$: 451.1456, found: 451.1455. *Syn*-**5cc**: white solid (827 mg, 41%): m.p. 93–94 °C, R_f (30% EtOAc/petrol ether) 0.13; ^{1}H NMR: δ 1.07 (dt, 3H, $^3J_{HH}$ = 7.1 Hz, $^4J_{HP}$ = 1.0 Hz, CH_3CH$_2$), 1.24 (dt, 3H, $^3J_{HH}$ = 7.1 Hz, $^4J_{HP}$ = 1.1 Hz, CH_3CH$_2$), 2.32 (s, 3H, C$_{Ar}$CH_3), 2.38 (s, 3H, C$_{Ar}$CH_3), 3.55 (br s, 1H, O*H*), 3.70–3.85 (m, 2H, CH_2), 3.97–4.14 (m, 2H, CH_2), 4.46–4.53 (m, 1H, C*H*OH), 5.85–5.93 (m, 1H, C*H*OP), 7.12 (d, 2H, $^3J_{HH}$ = 7.9 Hz, C$_{Ar}$*H*), 7.20 (d, 2H, $^3J_{HH}$ = 7.9 Hz, C$_{Ar}$*H*), 7.25 (d, 2H, $^3J_{HH}$ = 8.0 Hz, C$_{Ar}$*H*), 7.50 (d, 2H, $^3J_{HH}$ = 7.9 Hz, C$_{Ar}$*H*); ^{13}C NMR: δ 15.8 (d, $^3J_{CP}$ = 7.1 Hz, *C*H$_3$CH$_2$), 15.9 (d, $^3J_{CP}$ = 7.1 Hz, *C*H$_3$CH$_2$), 21.2 (s, C$_{Ar}$*C*H$_3$), 21.3 (s, C$_{Ar}$*C*H$_3$), 63.8 (d, $^2J_{CP}$ = 5.8 Hz, *C*H$_2$), 64.1 (d, $^2J_{CP}$ = 5.8 Hz, *C*H$_2$), 72.4 (dd, $^2J_{CF}$ = 30.4, 23.5 Hz, *C*HOH), 77.6–78.1 (m, *C*HOP), 119.7 (ddd, $^1J_{CF}$ = 257.3, 250.7 Hz, $^3J_{CP}$ = 7.3 Hz, *C*F$_2$), 127.9, 128.5, 128.8, 129.1, 130.8–130.9 (m), 133.2, 138.4, 139.3; ^{19}F NMR: δ −124.1 (ddd, 1F, $^2J_{FF}$ = 250.9 Hz, $^3J_{FH}$ = 19.4, 7.1 Hz),–122.6 (dd, 1F, $^2J_{FF}$ = 250.9 Hz, $^3J_{FH}$ = 16.6 Hz); ^{31}P NMR: δ–0.95 (s); GC–MS (EI) *m/z* 91 (40%), 119 (12), 154 (100), 254 (10); FTIR (film, ν_{max} cm^{-1}) 3329 (m), 3098 (w), 3030 (w), 2985 (m), 1616 (w), 1515 (m), 1256 (m), 1161 (m), 1029 (s); HRMS (ESI$^+$) calculated for $C_{21}H_{27}F_2NaO_5P$: 451.1456, found: 451.1455.

4.4.4. 1,3-Bis(4-methoxyphenyl)-2,2-difluoro-3-hydroxypropyl diethyl phosphate (**5dd**)

Prepared in analogy to **5cc** in 4 h reaction time, yielding separately *anti* and *syn* products in 1:1 ratio. *Anti*-**5dd**: colorless oil (258 mg, 39%): R_f (30% EtOAc/petrol ether) 0.17; ^{1}H NMR: δ 1.11 (dt, 3H, $^3J_{HH}$ = 7.1 Hz, $^4J_{HP}$ = 1.0 Hz, CH_3CH$_2$), 1.36 (dt, 3H, $^3J_{HH}$ = 7.1, $^4J_{HP}$ = 1.1 Hz, CH_3CH$_2$), 3.76 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 3.81–3.88 (m, 1H, CH_aH$_b$), 3.89–3.96 (m, 1H, CH$_a$$H_b$), 4.12–4.24 (m, 2H, C$H_2$), 5.06–5.13 (m, 1H, C*H*OH), 5.33 (br s, 1H, O*H*), 5.67–5.76 (m, 1H, C*H*OP), 6.86–6.89 (m, 4H, C$_{Ar}$*H*), 7.36–7.40 (m, 4H, C$_{Ar}$*H*); ^{13}C NMR: δ 15.8 (d, $^3J_{CP}$ = 6.8 Hz, *C*H$_3$CH$_2$), 16.0 (d, $^3J_{CP}$ = 6.7 Hz, *C*H$_3$CH$_2$), 55.1 (s, OCH$_3$), 55.2 (s, OCH$_3$), 64.8 (d, $^2J_{CP}$ = 6.3 Hz, CH$_2$), 64.9 (d, $^2J_{CP}$ = 6.1 Hz, CH$_2$), 70.6 (dd, $^2J_{CF}$ = 29.5, 25.8 Hz, *C*HOH), 75.1–75.7 (m, *C*HOP), 113.4, 113.7, 119.4 (dt, $^1J_{CF}$ = 252.2 Hz, $^3J_{CP}$ = 7.7 Hz, *C*F$_2$), 124.8 (d, $^3J_{CP}$ = 2.5 Hz), 128.0, 129.3, 129.8, 159.7, 160.4; ^{19}F NMR: δ −122.6 to −122.5 (m); ^{31}P NMR: δ 0.74 (s); FTIR (film, ν_{max} cm^{-1}) 3342 (m), 3070 (w), 3039 (w), 2985 (m), 2840 (w), 1614 (m), 1587 (w), 1515 (s), 1252 (s), 1178 (m), 1165 (m), 1032 (s); HRMS (ESI$^+$) calculated for $C_{21}H_{27}F_2NaO_7P$: 483.1355, found: 483.1354. *Syn*-**5dd**: colorless oil (260 mg, 40%): R_f (30% EtOAc/petrol ether) 0.06; ^{1}H NMR: δ 1.05 (dt, 3H, $^3J_{HH}$ = 7.1 Hz, $^4J_{HP}$ = 1.0 Hz, CH_3CH$_2$), 1.23 (dt, 3H, $^3J_{HH}$ = 7.1 Hz, $^4J_{HP}$ = 1.1 Hz, CH_3CH$_2$), 3.69–3.79 (m, 2H, CH_2), 3.76 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 3.96–4.09 (m, 2H, CH_2), 4.25 (d, 1H, $^3J_{HH}$ = 5.0 Hz, O*H*), 4.39–4.47 (m, 1H, C*H*OH), 5.86–5.95 (m, 1H, C*H*OP), 6.82 (d, 2H, $^3J_{HH}$ = 8.8 Hz, C$_{Ar}$*H*), 6.92 (d, 2H, $^3J_{HH}$ = 8.8 Hz, C$_{Ar}$*H*), 7.28 (d, 2H, $^3J_{HH}$ = 9.0 Hz, C$_{Ar}$*H*), 7.54 (d, 2H, $^3J_{HH}$ = 8.6 Hz, C$_{Ar}$*H*); ^{13}C NMR: δ 15.8 (d, $^3J_{CP}$ = 7.1 Hz, *C*H$_3$CH$_2$), 15.9 (d, $^3J_{CP}$ = 7.1 Hz, *C*H$_3$CH$_2$), 55.2 (s, OCH_3), 55.3 (s, OCH_3), 63.8 (d, $^2J_{CP}$ = 5.8 Hz, *C*H$_2$), 64.1 (d, $^2J_{CP}$ = 5.9 Hz, *C*H$_2$), 72.1 (dd, $^2J_{CF}$ = 30.1, 23.8, *C*HOH), 77.5–78.0 (m, *C*HOP), 113.5, 113.9, 120.0 (ddd, $^1J_{CF}$ = 257.0, 250.4 Hz, $^3J_{CP}$ = 7.2 Hz, *C*F$_2$), 126.0–126.1 (m), 128.6, 129.4, 130.1, 159.8, 160.4; ^{19}F NMR: δ −124.2 (ddd, 1F, $^2J_{FF}$ = 251.5 Hz, $^3J_{FH}$ = 18.8, 7.7 Hz),–122.4 (dd, 1F, $^2J_{FF}$ = 251.5 Hz, $^3J_{FH}$ = 16.4 Hz); ^{31}P NMR ($CDCl_3$) δ −0.96 (s); FTIR (film, ν_{max} cm^{-1}) 3329 (s), 3071 (w), 3040 (w), 2985 (m), 2840 (m), 1614 (s), 1586 (m), 1515 (s), 1252 (s), 1178 (s), 1162 (m), 1032 (s); HRMS (ESI$^+$) calculated for $C_{21}H_{27}F_2NaO_7P$: 483.1355, found: 483.1354.

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