Synthesis of Polyfluorinated Nitrogen-Containing Heterocycles from Hemifluorinated Enones or Organofluorosilicon Building Blocks as Synthetic Equivalents[‡]

Frédéric Chanteau,[a] Benoît Didier,[a] Boniface Dondy,[a] Pascale Doussot,[a] Richard Plantier-Royon,[a] and Charles Portella*[a]

Keywords: Acylsilanes / Michael addition / Nitrogen heterocycles / Organofluorine / Silyl enol ethers

A series of polyfluorinated heterocycles has been prepared by heterocyclisation of hemifluorinated enones or organofluorosilicon synthetic equivalents with different bis(nucleophiles). These polyfluorinated building blocks were obtained by treatment of acylsilanes with perfluoro organometallic reagents. The method is general and has been applied to aliphatic, aromatic and carbohydrate derivatives, to give oxazolidines, imidazolidines, benzodia- and -thiazepines, quinolines and pyrimidines bearing both a fluorine atom and a perfluoroalkyl group in vicinal positions.

Introduction

Development of an efficient method for the synthesis of fluorinated heterocyclic compounds is currently an important subject, as they often exhibit biological and physiological activities.[1] In particular, nitrogen-containing heterocyclic compounds play important roles in agrochemical and pharmaceutical fields.[2] Although there are good general reviews relating to the formation of pyrimidines, benzodiazepines and benzothiazepines,[3] the corresponding fluorine-containing heterocycles have been less studied. In addition, much attention has been focused on the synthesis and biological properties of heterocyces attached to a cyclic or acyclic sugar backbone[4] as nucleoside analogues.

The direct introduction of fluorine or perfluoroalkyl groups into heterocyclic structures can be achieved through the use of fluorinating or perfluoroalkylating reagents,[5] but the fluorinated building blocks strategy,[6] allowing classical condensation reactions, is more widely used, as in the following examples relating to the type of heterocycles described in this paper.

Trifluoromethylated imidazolidines and oxazolidines have been obtained by heterocyclisations of 3-trifluoroacetyl lactams with ethylenediamine and 2-aminoethanol without opening of the lactam structure.[7] Polyfluoro-2-alkynoic acids readily underwent intermolecular-intramolecular Michael addition reactions with a variety of bifunctional azanucleophiles to give the corresponding 2-(polyfluoroalkyl)imidazolidines and -oxazolidines.[8] The formation of polyfluorinated *N*,*N*′-unsubstituted imidazolidines was also carried out by treatment of heteroaromatic β-amino-β-(polyfluoroalkyl)vinyl ketones with ethylenediamine.[9]

Perfluoroalkylated 1,4-diazepines have been prepared by direct condensation of perfluoroalkyl-1,3-dicarbonyl compounds with ethylenediamine[10] or *o*-phenylenediamine.[11] α-Perfluoroalkylidene ketones have also been used as 1,3-bis(electrophilic) intermediates for synthesis of this heterocycle type.[12]

Various methods for the synthesis of perfluoroalkylated pyrimidines have been proposed. Beside classical reactions of amidines or guanidines with perfluoroalkylated 1,3-dicarbonyl systems[13] or the corresponding β-enaminone,[14] some particular approaches have been reported. The synthesis of 2,6-disubstituted 4-(trifluoromethyl)pyrimidines was accomplished by treatment of α,β-unsaturated trifluoromethyl ketones with amidines followed by a tandem dehydration-oxidation sequence.[15] α-Perfluoroalkylidene ketones proved to be versatile building blocks, potentially preparable in situ, to yield 4-(perfluoroalkyl)pyrimidines by direct condensation[12] or through treatment of the corresponding enaminoimine with orthoesters.[16] The synthesis of 5-fluoro-4-(perfluoroalkyl)pyrimidines is of particular interest in the context of this paper. These compounds were prepared by treatment of perfluoroalkenyl phosphates with amidinium salts.[17]

Previous papers in this series have demonstrated the versatility of treatment of perfluoroorganometallic reagents with acylsilanes to afford the 1-trialkylsilyl-1-perfluoro-

[‡] Mixed Organofluorine-Organosilicone Chemistry, 13. Part 12: Ref.[28]

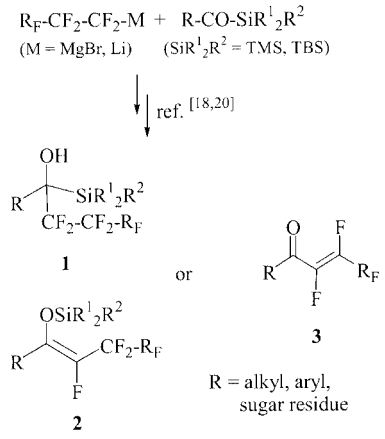
[a] UMR 6519 "Réactions Sélectives et Applications", CNRS – Université de Reims Champagne-Ardenne, UFR Sciences, B.P. 1039, 51687 Reims Cedex 2, France
Fax: (internat.) + 33-3-26913166
E-mail: charles.portella@univ-reims.fr

  DOI: 10.1002/ejoc.200300671

alkyl-alkan-1-ols **1**, the 1-alkyl-1-(trialkylsilyloxy)perfluoroalk-1-enes **2** and the corresponding hemifluorinated enones **3**.[18] In a preliminary account, we showed that these compounds behaved as synthetic equivalents. Treatment of any one of these compounds with bis(nucleophiles) gave various nitrogen-containing heterocycles.[19] In a more recent paper we described the synthesis of polyfluorinated pyrazoles through treatment with methylhydrazine.[20] This paper is a full account of the synthesis of various polyfluorinated heterocycles (imidazolidines, oxazolidines, benzodia- or thiazepines, quinolines and pyrimidines) bearing both a fluorine and a perfluoroalkyl substituent in vicinal positions and its extension to the synthesis of polyfluorinated heterocycles grafted onto a carbohydrate backbone.

Synthesis of Hemifluorinated Enones 3

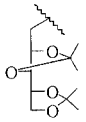
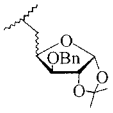
The overall process for the formation of the hemiperfluoroenones **3** from perfluoroalkyl iodides and acylsilanes has been described previously.[18b,20a] Depending on the experimental conditions, compounds **1**[18d,20b] and **2**[18a] can also be isolated and these two compounds are useful synthons that can be regarded as equivalents of the enones **3** (Scheme 1).

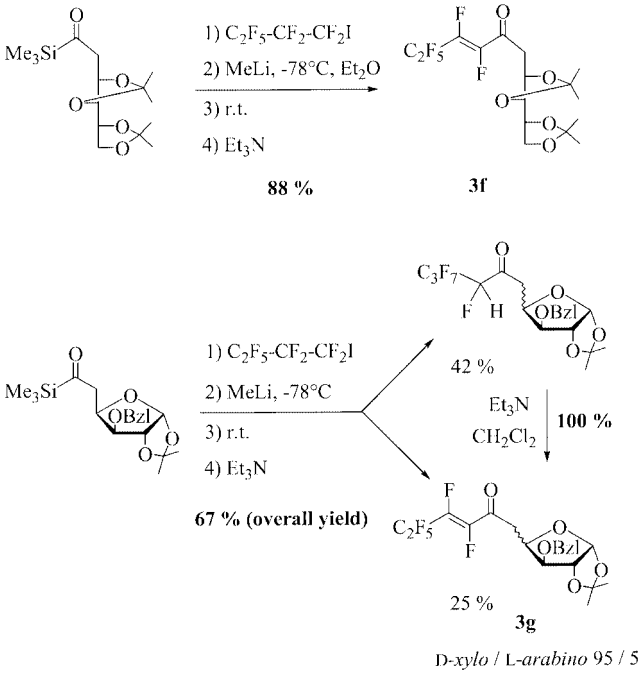


Scheme 1

In the carbohydrate series, synthesis of the enones **3f** and **3g** was achieved by the same procedure. Compound **3f** was obtained in a high yield from the corresponding acylsilane, synthesised by our reported procedure[21] from 2,3:4,5-di-*O*-isopropylidene-D-xylitol, obtained in turn by $NaBH_4$ reduction of diacetone-D-xylose.[22] A small amount (12%) of the hydroperfluoroketone, as a 50:50 mixture of diastereomers, resulting from the hydrolysis of the remaining enoxysilane **2**, was also obtained and separated by silica gel flash chromatography.[23] For the D-xylofuranose derivative, we observed a partial epimerisation (5%, determined after separation by HPLC and by integration of the anomeric protons in ^1H NMR or of CF_3 groups in ^{19}F NMR) at C-4 during the reaction. The reaction produced a mixture of the enone and the corresponding hydroperfluoroketone (Scheme 2). The two compounds were present as epimeric mixtures in the same 95:5 ratio (major D-*xylo* and minor L-*arabino*). This epimerisation at C-4 can be explained by the reversible opening of the furan ring after deprotonation at C-5 with one of the basic species present in the mixture. The same ratio of epimers was observed whatever the reaction conditions: (i) suppression of triethylamine to activate the

Table 1. Preparation of the starting compounds **1**–**3** through treatment of the acylsilanes with perfluoroorganometallic reagents

Compound	R	R^1	R^2	R_F	Yield (%)
1a	Ph	Me	Me	C_4F_9	97
3a	Ph	Me	Me	C_4F_9	88
1b	*p*-Cl-Ph	Me	Me	C_4F_9	80
3b	*p*-Cl-Ph	Me	Me	C_4F_9	91
1c	*p*-F-Ph	Me	Me	C_4F_9	84
3c	*p*-F-Ph	Me	Me	C_4F_9	89
1d	*p*-MeO-Ph	Me	Me	C_4F_9	84
3d	*p*-MeO-Ph	Me	Me	C_4F_9	87
2e	C_5H_{11}	Me	*t*-Bu	C_4F_9	90
3f		Me	Me	C_2F_5	88
3g		Me	Me	C_2F_5	67



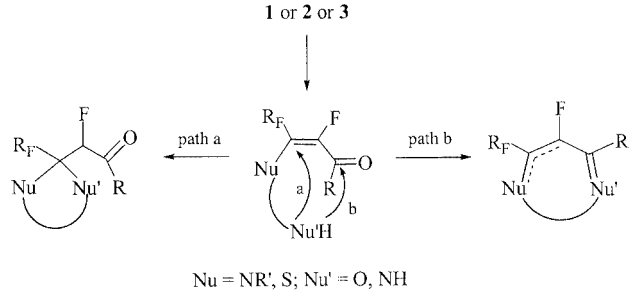
Scheme 2

conversion into the enone, the latter being formed under the action of the fluoride ion released in situ,[18b] or (ii) use of less than one equivalent of MeLi (0.9 equivalent) for the halogen-metal exchange step affording the perfluoroalkyllithium reagent. Although the starting acylsilane is no longer present in the medium at the time of introduction of triethylamine, we have observed that its treatment in diethyl ether at room temperature for 2 h induced epimerisation into the L-*arabino* epimer to about the same extent. These experiments show that either of these basic species, including the perfluoroalkyllithium reagent, are able to induce the observed epimerisation, probably at the enone stage.

The hydroperfluoro ketone can be separated by flash chromatography and is quantitatively converted into the corresponding enone **3g** by treatment with triethylamine in dichloromethane at room temperature, with the same ratio of the two epimers.[23] The two epimeric enones may be separated by HPLC (silica gel, eluent: hexane/EtOAc, 90:10), but owing to the possible epimerisation during the synthesis of the heterocycles (vide infra) the mixture of epimers was used in the following syntheses.

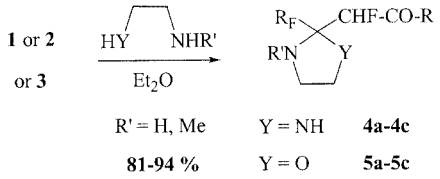
Synthesis of Fluorinated Imidazolidines, Oxazolidines, Benzodiazepines and Benzothiazepines

Generally, the cyclisation step giving rise to heterocycles from β-enaminone-type intermediates occurs at the carbonyl carbon atom.[24] Fluorine substitution strongly enhances the electrophilic properties of unsaturated substrates by modifying the charge distribution and lowering the LUMO level to a large extent.[25] Thus, for bis(nucleophilic) reagents able to give non-strained heterocycles, intramolecular nucleophilic attack in the intermediate enaminone is to be expected at either of the two electrophilic sites: the β-carbon (path a: Michael type addition) and/or the carbonyl carbon atom (path b: condensation). Some examples of such duality from fluorinated enone-type substrates have been reported (Scheme 3).[26]



Scheme 3

In contrast to these examples in which mixtures are produced, our substrates specifically gave one of the two possible cyclisation products.[19] Imidazolidines **4** are the unique products from the smooth reactions between 1,2-diaminoethanes and alcohol **1**, enoxysilane **2**, or enone **3**. Similarly, treatment of **1** or **2** with ethanolamines specifically gave the corresponding oxazolidines **5**. Results are summarised in Scheme 4 and Table 2.



Scheme 4

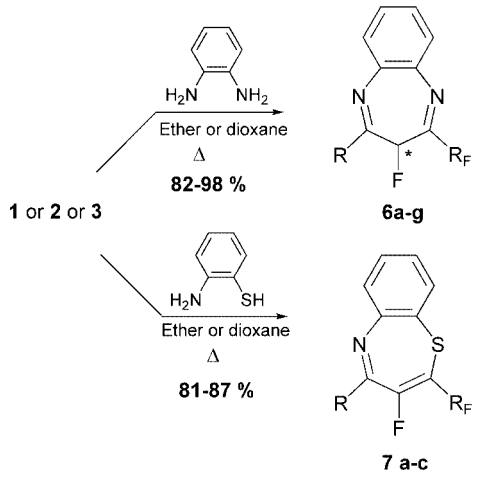
Table 2. Preparation of imidazolidines **4a−c** and oxazolidines **5a−c**

Entry	Starting compound	R^F	Y	R′	Yield (%)[a] Ratio of diastereomers
1	**1a**	C_4F_9	NH	H	**4a** (88)
2	**3a**	C_4F_9	NH	H	**4a** (92)
3	**1a**	C_4F_9	NH	Me	**4b** (81) 75:25
4	**3a**	C_4F_9	NH	Me	**4b** (88) 75:25
5	**2e**	C_4F_9	NH	H	**4c** (94)
6	**1a**	C_4F_9	O	H	**5a** (91) 62:38
7	**1a**	C_4F_9	O	Me	**5b** (92) 72:28
8	**2e**	C_4F_9	O	Me	**5c** (85) 91:9

[a] Pure isolated compounds.

The regioselectivity of the cyclisation was reversed with *o*-phenylenediamine, which exclusively gave the benzodiazepine **6**. The formation of a five-membered ring is hindered by the rigidity of this diamine and/or disfavoured frontier orbital interactions (if it is assumed that frontier orbital perturbation is the main parameter governing the regioselectivity). As reported in our preliminary account,[19] the synthesis of polyfluorinated benzodiazepines was directly performed from **1** or **2** and *o*-phenylenediamine. In the carbohydrate series, the best results were obtained by treatment of the hemiperfluoroenones **3** at reflux in diethyl ether or dioxane with an excess of *o*-phenylenediamine to give good yields of the corresponding benzodiazepines (Scheme 5, Table 3). From enone **3f**, a mixture of the diastereomers (50:50, 84%) was obtained after flash chromatography. From enone **3g** (as a mixture of two epimers D-*xylo*/L-*arabino*, 95:5) the two diastereoisomers (50:50, 88%) were obtained for each epimer. NMR spectra showed the exclusive formation of the diimine tautomer (^{1}H NMR, δ = 6.4 ppm, $^2J_{H,F}$ = 45 Hz. ^{13}C NMR, δ = 138 ppm, $^1J_{C,F}$ = 270 Hz).

The same reaction conditions were applied to 2-aminothiophenol, condensation of which with the enones **3** provided the corresponding benzothiazepines **7** in good yields (Scheme 5, Table 3).[19] The structure of the benzothiazepine was confirmed by NMR studies. ^{1}H NMR monitoring of the reaction showed the disappearance of the SH group before the NH_2 group in the first step. Concomitant disappearance of the fluorine atom in the β-position of the enone was confirmed by ^{19}F NMR monitoring. These observations indicate a prior attack of the more nucleophilic sulfur atom on the β carbon. In the carbohydrate series, the benzothiazepine **7c** was obtained as an epimeric mixture (D-*xylo*/L-*arabino* in a 85:15 ratio), indicating that a further C-



Scheme 5

Table 3. Preparation of benzodiazepines **6a**−**g** and benzothiazepines **7a**−**c**

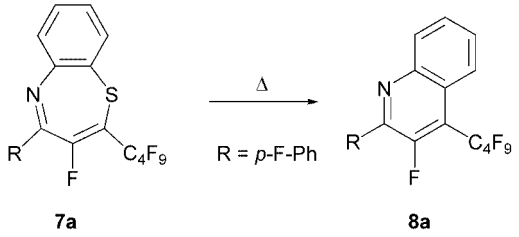
Entry	Starting compound	R_F	Yield (%)
1	**1a**	C_4F_9	**6a** (92)
2	**1b**	C_4F_9	**6b** (98)
3	**1c**	C_4F_9	**6c** (82)
4	**1d**	C_4F_9	**6d** (82)
5	**2e**	C_4F_9	**6e** (91)
6	**3f**	C_2F_5	**6f** (84)[a]
7	**3g**	C_2F_5	**6g** (88)[b]
8	**3c**	C_4F_9	**7a** (87)
9	**3f**	C_2F_5	**7b** (81)
10	**3g**	C_2F_5	**7c** (79)[c]

[a] Mixture (50:50) of diastereomers. [b] Mixture (50:50) of diastereomers for each epimer. [c] Mixture of the two epimers (D-*xylo*/L-*arabino*, 85:15).

4 epimerisation had occurred during the formation of the heterocycle.

Synthesis of Fluorinated Quinolines

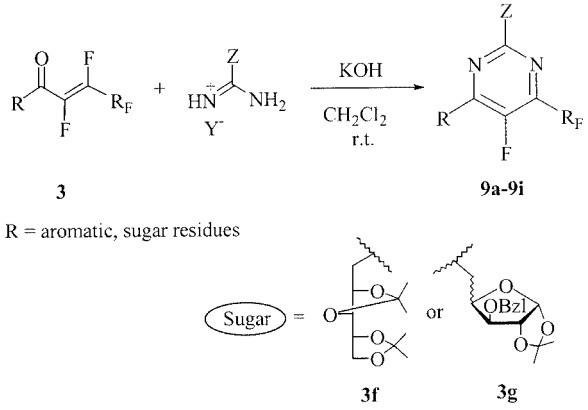
Literature results show that benzothiazepine structures are quite unstable and, under basic conditions or on heating, can be transformed into quinoline rings **8** by elimination of the sulfur atom.[27] In our hands, on heating to 120 °C, we observed an efficient extrusion of sulfur atom for the benzothiazepine with the aromatic substituent (Scheme 6). In the carbohydrate series, similar treatment resulted in the degradation of the starting materials **6f** and **6g**.



Scheme 6

Synthesis of Fluorinated Pyrimidines

Pyrimidines are conventionally synthesised by a [3+3] fragment approach involving amidines and substrates containing 1,3-dielectrophilic centres. In our hands, pyrimidines were obtained under mild basic conditions from hemiperfluoroenones **3** and various amidinium salts. From aromatic enones, different basic conditions were used: Et_3N/THF, diisopropylethylamine/THF and a KOH suspension in CH_2Cl_2, the last of these sets of conditions giving the best yields. The reaction was then extended to the D-xylose-derived enones **3f** and **3g** to give the pyrimidines **9d**−**9i** attached to carbohydrate moieties (Scheme 7, Table 4). In the D-xylofuranose series, the first experiments were carried out with the mixture of the two epimers (D-*xylo*/L-*arabino*) to give the corresponding pyrimidines in good yields. Once again, differences in the ratios of the two epimers were observed (D-*xylo*/L-*arabino*, 88:12 vs. 94:6). To confirm that a further epimerisation had taken place during the heterocycle formation process, the same reaction was carried out with the pure D-*xylo* epimer of the enone **3g** and *O*-methylisourea. The expected pyrimidine and its L-*arabino* epimer were obtained in a ratio of 88:12. They were separated by HPLC (silica gel, eluent: hexane/EtOAc, 90:10).



Scheme 7

Table 4. Preparation of pyrimidines **9a**−**i**

Entry	Starting compound	R_F	Z	Y	Yield (%)
1	**1c**	C_4F_9	H	AcO^-	**9a** (80)
2	**3f**	C_2F_5	H	AcO^-	**9b** (58)
3	**3f**	C_2F_5	Me	Cl^-	**9c** (64)
4	**3f**	C_2F_5	OMe	0.5 SO_4^{2-}	**9d** (78)
5	**3f**	C_2F_5	NH_2	Cl^-	**9e** (66)
6	**3g**	C_2F_5	H	AcO^-	**9f** (65)[a]
7	**3g**	C_2F_5	Me	Cl^-	**9g** (74)[a]
8	**3g**	C_2F_5	OMe	0.5 SO_4^{2-}	**9h** (75)[a]
9	**3g**	C_2F_5	NH_2	Cl^-	**9i** (66)[a]

[a] Yields given for the mixture of the two epimers D-*xylo*/L-*arabino*

It is interesting to compare our results with those reported by Ishihara,[17] who used perfluoroenol phosphates as intermediates towards pyrimidines with the same substi-

tution patterns. The authors pointed out that these enol phosphates are convenient synthetic equivalents of hemifluorinated enones, which should be compared to the silyl enol ether precursors of the enones in our methodology.

Conclusion

This paper reports and demonstrates the potential of the mixed organofluorosilicon synthons **1**, **2** and hemifluorinated enones **3** in the synthesis of elaborated fluoro-substituted systems such as nitrogen heterocycles. After the recently reported pyrazoles, polyfluorinated imidazolidines, oxazolidines, benzodia- and -thiazepines, quinolines and pyrimidines have been synthesised, and the procedure has been applied to aliphatic, aromatic and carbohydrate-derived substrates. The essential feature of these syntheses is undoubtedly the mild conditions required and the good yields generally obtained, thanks to the one-pot multistep process. An extension of this chemistry to new carbohydrate-derived acylsilanes with application to polyfluorinated homo-C-nucleosides analogues is described in a forthcoming paper.[28]

Experimental Section

Melting points are uncorrected. Optical rotations were determined with a Perkin−Elmer Model 241 polarimeter. FT-IR spectra were recorded with a MIDAC Corporation Spectrafile IR™ apparatus. ^{1}H, ^{13}C and ^{19}F spectra were recorded with Bruker AC 250 or AC 500 instruments in $CDCl_3$ as the solvent. Tetramethylsilane (δ = 0.00 ppm) or $CHCl_3$ (δ = 7.27 ppm) were used as internal standards for ^{1}H and ^{13}C NMR spectra and $CFCl_3$ for ^{19}F NMR spectra. MS data were obtained with a AUTOSPEC (VG Instruments) apparatus at 70 eV in the electron impact mode. Elemental analyses were performed with a Perkin−Elmer CHN 2400 apparatus. All reactions were monitored by TLC (Merck silica gel F 254). Silica gel (Merck 9385, 40−63μm) was used for flash chromatography. HPLC separations were performed on a HP 1100 Series chromatograph with a LiChrospher Si60 (5μm) column. All reactions were carried out under dry argon. THF was dried and freshly distilled from over sodium/benzophenone. Diethyl ether (SDS Purex for analyses) was used without further purification.

The syntheses and characterisation of the following substrates have been reported: aromatic and aliphatic acylsilanes,[18c] D-xylose-derived acylsilanes,[21] alcohols **1a**−**1d**,[18c] enolsilyl ether **2e**,[18a] and enones **3a**−**d**.[18b]

Preparation of Carbohydrate-derived Hemiperfluoroenones 3f and 3g

(*E*)-1-(1′-Deoxy-2′,3′:4′,5′-di-*O*-isopropylidene-D-xylityl)-2,3,4,4,5,5,5-heptafluoropent-2-en-1-one (3f): Freshly distilled perfluorobutyl iodide (0.93 mL, 5.6 mmol, 1.2 equiv.) was added to a solution of the acylsilane (1.5 g, 4.7 mmol, 1.0 equiv.) in diethyl ether (20 mL). After the mixture had been cooled to −78 °C, a solution of methyllithium (5.6 mmol, 1.2 equiv.) in diethyl ether was added dropwise. The mixture was stirred at −78 °C for 30 min and was then warmed to room temperature (3 h). Triethylamine (3.1 mL, 23.5 mmol, 5 equiv.) was added, and the resulting mixture was stirred overnight. After dilution with diethyl ether (50 mL) and hydrolysis with saturated aqueous NH_4Cl solution, the crude product was extracted with diethyl ether (3 × 20 mL). The combined organic phases were dried with $MgSO_4$, filtered and concentrated in vacuo. The residue was chromatographed on silica gel (petroleum ether/EtOAc, 90:10) to give the hemifluorinated enone as an oil (1.75 g, 88%). The corresponding hydroperfluoro ketone was also isolated (0.25 g, 12%). ^{1}H NMR: δ = 1.33 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3), 1.39 (s, 3 H, CH_3), 2.96 (ddd, $^2J_{1',1''}$ = 16.8, $^3J_{1',2'}$ = 4.2, $^4J_{1',F'}$ = 2.3 Hz, 1 H, 1′-H), 3.06 (ddd, $^2J_{1'',1'}$ = 16.8, $^3J_{1'',2'}$ = 7.6, $^4J_{1'',F'}$ = 2.3 Hz, 1 H, 1′′-H), 3.81 (dd, $^3J_{3',2'}$ = 7.6, $^3J_{3',4'}$ = 3.8 Hz, 1 H, 3′-H), 3.86 (dd, $^2J_{5',5''}$ = 8.4, $^3J_{5',4'}$ = 7.2 Hz, 1 H, 5′-H), 4.03 (dd, $^2J_{5'',5'}$ = 8.4, $^3J_{5'',4'}$ = 6.9 Hz, 1 H, 5′′-H), 4.21 (dt, $^3J_{4',3'}$ = 3.8, $^3J_{4',5'}$ = 6.9, $^3J_{4',5''}$ = 6.9 Hz, 1 H, 4′-H), 4.44 (dt, $^3J_{2',3'}$ = 7.6, $^3J_{2',1'}$ = 4.2, $^3J_{2',1''}$ = 7.6 Hz, 1 H, 2′-H) ppm. ^{13}C NMR: δ = 25.1 (s, CH_3), 25.2 (s, CH_3), 25.9 (s, CH_3), 26.7 (s, CH_3), 43.9 (s, CH_2, C-1′), 65.4 (s, CH_2, C-5′), 72.0 (s, CH, C-4′), 74.6 (s, CH, C-2′), 80.6 (s, CH, C-3′), 109.8−110.0 (s, $C_{q,acet.}$), 110.4−112.0 (m, 2 C, CF-2, CF-3), 117.8 (qt, $^1J_{C,F}$ = 286.5, $^2J_{C,F}$ = 37.4 Hz, CF_3), 146.0 (tq, $^1J_{C,F}$ = 235.8, $^2J_{C,F}$ = 37.4 Hz, CF_2), 188.1 (d, $^2J_{C,F}$ = 21.6 Hz, C=O) ppm. ^{19}F NMR: δ = −84.8 (m, 3 F, CF_3), −121.8 (dd, *J* = 22.9, *J* = 7.6 Hz, 2 F, CF_2), −151.4 (d, *J* = 137.3 Hz, 1 F, CF-2), −152.3 (ddt, *J* = 137.3, *J* = 22.9, *J* = 7.6 Hz, 1 F, CF-3) ppm. IR (film): ṽ = 2990, 2938, 1736, 1382, 1227, 1072, 858 cm^{-1}. MS: *m*/*z* (%) = 424 (23) [M$^+$], 409, 309, 291, 264, 248, 241, 209, 201, 143. $C_{16}H_{19}F_7O_5$: calcd. C 45.29, H 4.51; found C 45.09, H 4.39.

(*E*)-1-(3′-*O*-Benzyl-5′-deoxy-1′,2′-*O*-isopropylidene-α-D-xylofuranosyl)-2,3,4,4,5,5,5-heptafluoropent-2-en-1-one (3g, major diastereomer): Freshly distilled perfluorobutyl iodide (0.44 mL, 2.6 mmol, 1.2 equiv.) was added to a solution of the acylsilane (0.8 g, 2.2 mmol, 1.0 equiv.) in diethyl ether (12 mL). After the mixture had been cooled to −78 °C, a solution of methyllithium (2.6 mmol, 1.2 equiv.) in diethyl ether was added dropwise. The mixture was stirred at −78 °C for 30 min and was then warmed to room temperature (3 h). Triethylamine (1.72 mL, 13 mmol, 5 equiv.) was added, and the resulting mixture was stirred overnight. After dilution with diethyl ether (50 mL) and hydrolysis with saturated aqueous NH_4Cl solution, the crude product was extracted with diethyl ether (3 × 20 mL). The combined organic phases were dried with $MgSO_4$, filtered and concentrated in vacuo. The residue was chromatographed on silica gel (petroleum ether/EtOAc, 95:5) to give a mixture of the two epimeric (D-*xylo*/L-*arabino*, 95:5) hemifluorinated enones. A small amount of the major epimer was purified by HPLC (silica gel, eluent: cyclohexane/EtOAc, 90:10, 3 mL/min). ^{1}H NMR: δ = 1.36 (s, 3 H, CH_3), 1.53 (s, 3 H, CH_3), 3.10−3.25 (m, 2 H, 5′-H), 4.11 (d, $^3J_{3',4'}$ = 3.3 Hz, 1 H, 3′-H), 4.39 (d, $^2J_{H,H'}$ = 11.8 Hz, 1 H, H_{benzyl}), 4.66−4.70 (m, 2 H, 2′-H, 4′-H), 4.71 (d, $^2J_{H',H}$ = 11.8 Hz, 1 H, H'_{benzyl}), 5.92 (d, $^3J_{1',2'}$ = 3.8 Hz, 1 H, 1′-H), 7.22−7.38 (m, 5 H, $H_{arom.}$) ppm. ^{13}C NMR: δ = 26.2 (s, CH_3), 26.7 (s, CH_3), 39.7 (d, $^3J_{C,F}$ = 4.0 Hz, C-5′); 72.1 (s, CH_2 benzyl), 75.4 (s, CH, C-4′), 81.7 (s, C-3′), 82.2 (s, CH, C-2′), 104.6 (s, CH, C-1′), 111.8 (s, $C_{q,acet.}$), 117.9 (qt, $^1J_{C,F}$ = 287.4, $^2J_{C,F}$ = 35.4 Hz, CF_3), 127.8−128.1−128.5−128.6 ($CH_{arom.}$), 137.0 ($C_{q,arom.}$), 143.7 (dd, $^1J_{C,F}$ = 262.2, $^2J_{C,F}$ = 32.1 Hz, CF), 147.6 (dd, $^1J_{C,F}$ = 260.6, $^2J_{C,F}$ = 26.6 Hz, CF), 188.2 (d, $^2J_{C,F}$ = 23.6 Hz, C=O) ppm. ^{19}F NMR: δ = −84.5 (m, 3 F, CF_3), −121.5 (dm, $^3J_{F,F}$ = 23.3 Hz, 2 F, CF_2), −151.5 (d, $^3J_{F,F}$ = 137.3 Hz, 1 F, CF-2), −151.7 (dtm, $^3J_{F,F}$ = 137.3, $^3J_{F,F}$ = 23.3 Hz, 1 F, CF-3) ppm. MS: *m*/*z* (%) = 472 (15) [M$^+$], 457 [M − 15], 413, 307 (100), 249, 209. IR (film): ṽ = 2957, 1738, 1638, 1370, 1254, 1076, 851 cm^{-1}. $C_{20}H_{19}F_7O_5$ calcd. C 50.86, H 4.05; found C 50.80, H 4.10.

(*E*)-1-(3′-*O*-Benzyl-5′-deoxy-1′,2′-*O*-isopropylidene-β-L-arabinofuranosyl)-2,3,4,4,5,5,5-heptafluoropent-2-en-1-one (3g, minor diastereomer): ^{1}H NMR: δ = 4.09 (d, $^3J_{3',4'}$ = 2.0 Hz, 1 H, 3′-H), 5.93 (d, $^3J_{1',2'}$ = 3.6 Hz, 1 H, 1′-H) ppm. ^{13}C NMR: δ = 44.7 (d, $^3J_{C,F}$ = 3.2 Hz, C-5′) ppm. ^{19}F NMR: δ = −85.1 (m, 3 F, CF_3), −121.6 (m, 2 F, CF_2), −153.0 (d, $^3J_{F,F}$ = 137.3 Hz, 1 F, CF-2) ppm.

General Procedure for the Synthesis of Imidazolidines 4 and Oxazolidines 5 from 1: The bis(nucleophilic) compound (6 mmol, 3 equiv.) − ethylenediamine or *N*-methylethylenediamine for imidazolidines **4** and ethanolamine or *N*-methylethanolamine for oxazolidines **5** − was added to a solution of **1a** (2 mmol) in diethyl ether (20 mL). The mixture was stirred at reflux for 4 h and filtered. After solvent removal, compounds **4a**−**c** and **5a**−**c** were purified by silica gel chromatography (EtOAc/petroleum ether).

General Procedure for the Synthesis of Imidazolidines 4 and Oxazolidines 5 from 2: The bis(nucleophilic) compound (0.4 mmol, 2 equiv.) was added to a solution of **2e** (0.2 mmol) in diethyl ether (2 mL). The mixture was stirred at room temperature for 5 h and filtered. After solvent removal, compounds **4** and **5** were purified by silica gel chromatography (CH_2Cl_2/petroleum ether).

General Procedure for the Synthesis of Imidazolidines 4 and Oxazolidines 5 from 3: The bis(nucleophilic) compound (4 mmol, 2 equiv.) − ethylenediamine or *N*-methylethylenediamine for imidazolidines **4** and ethanolamine or *N*-methylethanolamine for oxazolidines **5** − was added to a solution of **3a** (2 mmol) in diethyl ether (20 mL). The mixture was stirred at reflux for 4 h and filtered. After solvent removal, compounds **4a**−**c** and **5a**−**c** were purified by silica gel chromatography (EtOAc/petroleum ether).

2-(1′-Fluoro-2′-oxo-2′-phenylethyl)-2-perfluorobutylimidazolidine (4a): ^{1}H NMR: δ = 2.75 (br. s, 2 H, NH), 3.03 (m, 4 H, CH_2−N), 5.90 (d, $^2J_{H,F}$ = 46.0 Hz, 1 H, 1′-H), 7.60 (m, 3 H, Ar), 7.90 (m, 2 H, Ar) ppm. ^{13}C NMR: δ = 45.6 (s, CH_2−N), 83.2 (m, C-1), 88.0 (d, $^1J_{C,F}$ = 194.0 Hz, C-1′), 127.7−136.2 ($C_{arom.}$), 194.9 (d, $^2J_{C,F}$ = 19.7 Hz, C-2′) ppm. ^{19}F NMR: δ = −81.3 (m, 3 F, CF_3), −113.6 (d, $^2J_{F,F}$ = 284.0 Hz, 1 F, 1F[a]), −114.9 (d, $^2J_{F,F}$ = 284.0 Hz, 1 F, 1 F[a]) −121.5 (m, 2 F, CF_2), −126.3 (m, 2 F, CF_2) ppm. IR (film): ṽ = 3400, 2990, 1680, 1590, 1200, 1030 cm^{-1}. MS: *m*/*z* (%) = 427 (10) [M$^+$ + 1], 289 (100), 207, 120, 105, 77. $C_{15}H_{12}F_{10}N_2O$: calcd. C 42.27, H 2.84, N 6.57; found C 42.25, H 2.67, N 6.12.

2-(1′-Fluoro-2′-oxo-2′-phenylethyl)-1-methyl-2-(perfluorobutyl)-imidazolidine (4b): Mixture of two diastereomers: 75:25. ^{1}H NMR (major diastereomer): δ = 1.55 (s, 1 H, NH), 2.80 (s, 4 H, CH_2−N), 3.05 (s, 3 H, N−CH_3), 5.80 (d, $^2J_{H,F}$ = 46.0 Hz, 1 H, 1′-H), 7.45 (m, 3 H, Ar), 7.95 (m, 2 H, Ar) ppm. ^{1}H NMR (minor diastereomer): δ = 1.55 (s, 1 H, NH), 2.50 (s, 4 H, CH_2−N), 3.05 (s, 3 H, N−CH_3), 5.50 (d, $^2J_{H,F}$ = 46.0 Hz, 1 H, 1′-H), 7.45 (m, 3 H, Ar), 7.95 (m, 2 H, Ar) ppm. ^{13}C NMR (major diastereomer): δ = 45.6 (s, CH_2−N), 55.4 (s, N−CH_3), 87.8 (d, $^1J_{C,F}$ = 194.7 Hz, C-1′), 127.7−136.0 ($C_{arom.}$), 194.8 (d, $^2J_{C,F}$ = 20.1 Hz, C-2′) ppm. ^{13}C NMR (minor diastereomer): δ = 45.4 (s, CH_2−N), 55.2 (s, N−CH_3), 83.1 (d, $^1J_{C,F}$ = 184.0 Hz, C-1′), 127.7−136.0 ($C_{arom.}$), 193.2 (d, $^2J_{C,F}$ = 20.1 Hz, C-2′) ppm. ^{19}F NMR (major diastereomer): δ = −81.3 (m, 3 F, CF_3), −113.2 (d, $^2J_{F,F}$ = 283.0 Hz, 1 F, 1F[a]), −114.7 (d, $^2J_{F,F}$ = 283.0 Hz, 1 F, 1F[a]) −121.6 (m, 2 F, CF_2), −126.4 (m, 2 F, CF_2) ppm. IR (film): ṽ = 3400, 3000, 1680, 1600, 1200, 1030 cm^{-1}. MS: *m*/*z* (%) = 440 (20) [M$^+$], 421, 363, 335, 323, 303 (100), 221, 105, 77.

2-(1′-Fluoro-2′-oxo-2′-heptyl)-2-(perfluorobutyl)imidazolidine (4c): ^{1}H NMR: δ = 0.90 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H, CH_3), 1.30 (m, 4 H, 2CH_2), 1.58 (q, $^3J_{H,H}$ = 7.0 Hz, 2 H, CH_2), 2.73 (m, 4 H, CH_2 + 2 NH), 3.00 (m, 2 H, CH_2−N), 3.15 (m, 2 H, CH_2−N), 4.82 (d, $^2J_{H,F}$ = 50.0 Hz, 1 H, 1′-H) ppm. ^{13}C NMR: δ = 13.8 (s, CH_3), 22.1, 22.4, 31.1 (3s, 3 CH_2), 40.3 (s, CH_2), 45.4 (s, CH_2−N), 45.6 (s, CH_2−N), 82.9 (q, $^2J_{C,F}$ = 19.0 Hz, C-1), 92.6 (d, $^1J_{C,F}$ = 197.0 Hz, C-1′), 208.6 (d, $^2J_{C,F}$ = 25.0 Hz, C-2′) ppm. ^{19}F NMR: δ = −81.3 (t, $^3J_{F,F}$ = 10.0 Hz, 3 F, CF_3), −116.4 (d, $^2J_{F,F}$ = 280.0 Hz, 1 F, 1F[a]), −117.8 (d, $^2J_{F,F}$ = 280.0 Hz, 1 F, 1F[a]) −121.5 (m, 2 F, CF_2), −126.4 (m, 2 F, CF_2), −195.7 (m, 1 F, CF-1′) ppm. IR (film): ṽ = 3430, 3000, 2860, 1720, 1660, 1460, 1230, 1140, 1040 cm^{-1}. MS: *m*/*z* (%) = 420 (12) [M$^+$], 405 (96), 389 (17), 343 (30), 327 (100), 253 (61), 193 (51), 193 (51), 156 (70), 135 (44), 91 (60). $C_{14}H_{18}F_{10}N_2O$: calcd. C 40.01, H 4.32, N 6.67; found C 40.22, H 4.22, N 6.59.

2-(1′-Fluoro-2′-oxo-2′-phenylethyl)-2-(perfluorobutyl)-1-oxazolidine (5a): Mixture of two diastereomers: 62:38. ^{1}H NMR (major diastereomer): δ = 3.13 (m, 2 H, CH_2−N), 3.35 (m, 1 H, CH_2−O), 3.50 (s, 1 H, NH), 3.88 (m, 1 H, CH_2−O), 6.25 (d, $^2J_{H,F}$ = 46.0 Hz, 1 H, 1′-H), 7.50 (m, 3 H, Ar), 7.90 (m, 2 H, Ar) ppm. ^{1}H NMR (minor diastereomer): δ = 3.25 (m, 2 H, CH_2−N), 3.50 (s, 1 H, NH), 3.63 (m, 1 H, CH_2−O), 4.05 (m, 1 H, CH_2−O), 5.63 (d, $^2J_{H,F}$ = 46.0 Hz, 1 H, 1′-H), 7.65 (m, 3 H, Ar), 8.10 (m, 2 H, Ar) ppm. ^{13}C NMR (major diastereomer): δ = 45.3 (s, CH_2−N), 68.2 (s, CH_2−O), 85.0 (d, $^1J_{C,F}$ = 191.4 Hz, C-1′), 96.5 (m, C-1), 127.7−136.0 ($C_{arom.}$), 193.3 (d, $^2J_{C,F}$ = 18.0 Hz, C-2′) ppm. ^{13}C NMR (minor diastereomer): δ = 45.5 (s, CH_2−N), 68.7 (s, CH_2−O), 91.0 (d, $^1J_{C,F}$ = 191.4 Hz, C-1′), 97.0 (d, $^2J_{C,F}$ = 30.0 Hz, C-1), 127.7−136.0 ($C_{arom.}$), 193.3 (d, $^2J_{C,F}$ = 18.0 Hz, C-2′) ppm. ^{19}F NMR (major diastereomer): δ = −81.3 (m, 3 F, CF_3), −121.4 (m, 2 F, 2F[a]), −122.3 (m, 2 F, CF_2), −126.4 (m, 2 F, CF_2), −196.3 (m, 1 F, CF-1′) ppm. ^{19}F NMR (minor diastereomer): δ = −81.3 (m, 3 F, CF_3), −117.4 (m, 2 F, 2F[a]), −121.6 (m, 2 F, CF_2), −126.4 (m, 2 F, CF_2), −193.9 (m, 1 F, CF-1′) ppm. IR (film): ṽ = 3360, 3000, 1690, 1600, 1450, 1350, 1200, 1130 cm^{-1}. MS: *m*/*z* (%) = 428 (15) [M$^+$], 410, 290, 209, 105 (100), 77. $C_{15}H_{11}F_{10}NO_2$: calcd. C 42.16, H 2.56, N 3.27; found C 42.20, H 2.61, N 3.09.

2-(1′-Fluoro-2′-oxo-2′-phenylethyl)-1-methyl-2-(perfluorobutyl)-oxazolidine (5b): Mixture of two diastereomers: 72:28. ^{1}H NMR (major diastereomer): δ = 2.80 (s, 3 H, N−CH_3), 3.05 (q, $J_{H,H}$ = 9.0 Hz, 1 H, CH_2−N), 3.15 (q, $J_{H,H}$ = 9.0 Hz, 1 H, CH_2−N), 3.40 (dq, $J_{H,H}$ = 9.0, $J_{H,H}$ = 2.0 Hz, 1 H, CH_2−O), 3.90 (dq, $J_{H,H}$ = 9.0, $J_{H,H}$ = 2.0 Hz, 1 H, CH_2−O), 6.10 (d, $^2J_{H,F}$ = 45.0 Hz, 1 H, 1′-H), 7.50 (m, 3 H, Ar), 7.90 (m, 2 H, Ar) ppm. ^{1}H NMR (minor diastereomer): δ = 2.70 (s, 3 H, N−CH_3), 3.00 (q, $J_{H,H}$ = 9.0 Hz, 1 H, CH_2−N), 3.13 (q, $J_{H,H}$ = 9.0 Hz, 1 H, CH_2−N), 3.55 (dq, $J_{H,H}$ = 9.0, $J_{H,H}$ = 2.0 Hz, 1 H, CH_2−O), 4.00 (dq, $J_{H,H}$ = 9.0, $J_{H,H}$ = 2.0 Hz, 1 H, CH_2−O), 5.60 (d, $^2J_{H,F}$ = 45.0 Hz, 1 H, 1′-H), 7.70 (m, 3 H, Ar), 8.00 (m, 2 H, Ar) ppm. ^{13}C NMR (major diastereomer): δ = 34.1 (s, N−CH_3), 52.8 (s, CH_2−N), 66.7 (s, CH_2−O), 91.7 (d, $^1J_{C,F}$ = 196.1 Hz, C-1′), 94.6 (m, C-1), 127.7−136.0 ($C_{arom.}$), 193.2 (d, $^2J_{C,F}$ = 19.0 Hz, C-2′) ppm. ^{13}C NMR (minor diastereomer): δ = 33.9 (s, N−CH_3), 51.7 (s, CH_2−N), 66.7 (s, CH_2−O), 92.8 (d, $^1J_{C,F}$ = 196.1 Hz, C-1′), 95.7 (m, C-1), 127.7−136.0 ($C_{arom.}$), 193.9 (d, $^2J_{C,F}$ = 19.0 Hz, C-2′) ppm. ^{19}F NMR (major diastereomer): δ = −81.3 (m, 3 F, CF_3), −117.5 (m, 2 F, 2F[a]), −121.8 (m, 2 F, CF_2), −126.6 (m, 2 F, CF_2), −194.0 (dm, $^2J_{F,H}$ = 46.0 Hz, 1 F, CF-1′) ppm. IR (film): ṽ = 3000, 1690, 1600, 1450, 1350, 1200, 1130 cm^{-1}. MS: *m*/*z* (%) = 442 (10) [M$^+$], 424, 304, 223, 219, 105 (100), 77.

2-(1′-Fluoro-2′-oxo-2′-heptyl)-2-(perfluorobutyl)-1-oxazolidine (5c): Mixture of two diastereomers: 91:9. ^{1}H NMR: δ = 0.85 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H, CH_3), 1.25 (m, 4 H, 2CH_2), 1.53 (q, $^3J_{H,H}$ = 7.0 Hz, 2 H, CH_2), 2.58 (dt, $^3J_{H,H}$ = 7.0, $^4J_{H,F}$ = 3.0 Hz, 4 H, CH_2), 2.64

(s, 3 H, N−CH_3), 3.00−3.25 (m, 2 H, CH_2−N), 4.05 (m, 2 H, CH_2−O), 4.95 (d, $^2J_{H,F}$ = 49.0 Hz, 1 H, 1′-H minor isomer), 5.07 (d, $^2J_{H,F}$ = 49.0 Hz, 1 H, 1′-H major isomer) ppm. ^{13}C NMR (major diastereomer): δ = 13.8 (s, CH_3), 22.1, 31.3, 39.3 (3s, 3 CH_2), 43.9 (s, N−CH_3), 53.4 (s, CH_2), 58.6 (s, CH_2−N), 67.2 (s, CH_2−O), 94.0 (d, $^1J_{C,F}$ = 194.0 Hz, C-1′), 204.6 (d, $^2J_{C,F}$ = 24.0 Hz, C-2′) ppm. ^{13}C NMR (minor diastereomer): δ = 15.2 (s, CH_3), 23.2, 29.7, 34.4 (3s, 3 CH_2), 39.6 (s, N−CH_3), 51.6 (s, CH_2), 56.3 (s, CH_2−N), 66.9 (s, CH_2−O), 92.0 (d, $^1J_{C,F}$ = 201.0 Hz, C-1′), 195.6 (d, $^2J_{C,F}$ = 35.0 Hz, C-2′) ppm. ^{19}F NMR: δ = −81.5 (t, $^3J_{F,F}$ = 10.0 Hz, 3 F, CF_3), −109.9 (m, 2 F, CF_2) −122.6 (m, 2 F, CF_2), −126.8 (m, 2 F, CF_2), −197.7 (m, 1 F, CF-1′) ppm. IR (film): ṽ = 3005, 2960, 2870, 1720, 1455, 1350, 1230, 1135, 1070, 1035 cm^{-1}. MS: *m*/*z* (%) = 435 (< 1) [M$^+$], 304 (100), 260 (7), 217 (11), 216 (97), 118 (44), 99 (11), 71 (10). $C_{15}H_{19}F_{10}NO_2$: calcd. C 41.39, H 4.40, N 3.22; found C 41.72, H 4.36, N 3.12.

General Procedure for the Synthesis of Benzodiazepines 6 from 1: *o*-Phenylenediamine (5 mmol, 5 equiv.) and $MgSO_4$ were added to a solution of **1** (1 mmol) in diethyl ether (20 mL). The mixture was stirred at reflux for 24 h and filtered. After solvent removal, compounds **6a**−**d** were purified by silica gel chromatography (petroleum ether/dichloromethane, 70:30).

General Procedure for the Synthesis of Benzodiazepines 6 from 2: 1,2-Phenylenediamine (0.4 mmol, 2 equiv.) was added to a solution of **2e** (0.2 mmol) in methanol (2 mL). The mixture was stirred overnight at 50 °C. After extraction with water and diethyl ether, compound **6e** was purified by silica gel chromatography (petroleum ether/dichloromethane, 90:10).

General Procedure for the Synthesis of Benzodiazepines 6 from 3: The *o*-phenylenediamine (10 mmol, 5 equiv.) and $MgSO_4$ were added to a solution of **3** (2 mmol) in diethyl ether or dioxane (20 mL). The mixture was stirred at room temperature overnight and filtered. The reaction mixture was washed with an aqueous solution of ammonium chloride, and the aqueous layer was extracted twice with 20 mL of diethyl ether. The organic layer was dried with $MgSO_4$ and filtered. After solvent removal, benzodiazepines **6f**−**g** were purified by silica gel chromatography (petroleum ether/EtOAc, 95:5).

3-Fluoro-2-(perfluorobutyl)-4-phenylbenzo-1,5-diazepine (6a): ^{1}H NMR: δ = 6.60 (d, $^2J_{H,F}$ = 45.0 Hz, 1 H, 3-H), 7.40−7.60 (m, 5 H, $H_{arom.}$), 7.75 (t, *J* = 7.6 Hz, 2 H, $H_{arom.}$), 8.00 (d, *J* = 7.6 Hz, 2 H, $H_{arom.}$) ppm. ^{13}C NMR: δ = 126.9−138.3 (m, $C_{arom.}$), 138.5 (d, $^1J_{C,F}$ = 268.6 Hz, C-3), 140.1 (s, C-2), 148.4 (s, C-4) ppm. ^{19}F NMR: δ = −81.4 (m, CF_3), −112.9 (m, CF_2), −122.3 (m, CF_2), −125.8 (m, CF_2), −196.0 (m, CF) ppm. IR (film): ṽ = 3000, 1700, 1680, 1600, 1570, 1510, 1470, 1410, 1220, 1160, 1090 cm^{-1}. MS: *m*/*z* (%) = 456 (20) [M$^+$], 237, 77. $C_{19}H_{10}F_{10}N_2$: calcd. C 50.01, H 2.21, N 6.14; found C 50.32, H 2.24, N 6.18.

4-(4′-Chlorophenyl)-3-fluoro-2-(perfluorobutyl)benzo-1,5-diazepine (6b): ^{1}H NMR: δ = 6.43 (d, $^2J_{H,F}$ = 45.0 Hz, 1 H, 3-H), 7.45−7.55 (m, 4 H, $H_{arom.}$), 7.75 (d, *J* = 7.6 Hz, 2 H, $H_{arom.}$), 7.96 (d, *J* = 7.6 Hz, 2 H, $H_{arom.}$) ppm. ^{13}C NMR: δ = 126.9−138.3 (m, $C_{arom.}$), 138.5 (d, $^1J_{C,F}$ = 268.6 Hz, C-3), 140.1 (s, C-2), 148.4 (s, C-4) ppm. ^{19}F NMR: δ = −81.4 (m, CF_3), −113.1 (m, CF_2^a), −122.4 (m, CF_2^b), −125.6 (m, CF_2^c), −195.8 (m, CF) ppm. IR (film): ṽ = 3010, 1710, 1680, 1600, 1590, 1510, 1410, 1230, 1140 cm^{-1}. MS: *m*/*z* (%) = 490 (10) [M$^+$], 371, 271, 111. $C_{19}H_9ClF_{10}N_2$: calcd. C 46.50, H 1.85, N 5.71; found C 46.95, H 2.06, N 5.42.

3-Fluoro-4-(4′-fluorophenyl)-2-(perfluorobutyl)benzo-1,5-diazepine (6c): ^{1}H NMR: δ = 6.35 (d, $^2J_{H,F}$ = 45.0 Hz, 1 H, 3-H), 7.15−7.30 (m, 2 H, $H_{arom.}$), 7.45 (t, *J* = 7.6 Hz, 1 H, $H_{arom.}$), 7.55 (t, *J* = 7.6 Hz, 1 H, $H_{arom.}$), 7.75 (d, *J* = 7.6 Hz, 2 H, $H_{arom.}$), 8.02 (d, *J* = 7.6 Hz, 1 H, $H_{arom.}$) ppm. ^{13}C NMR: δ = 126.0−131.0 (m, $C_{arom.}$), 138.5 (d, $^1J_{C,F}$ = 277.0 Hz, C-3), 140.4 (m, C-2), 148.3 (d, $^2J_{C,F}$ = 7.5 Hz, C-4), 164.9 (d, $^1J_{C,F}$ = 254.7 Hz, CF) ppm. ^{19}F NMR: δ = −81.4 (m, CF_3), −107.5 (m, $CF_{arom.}$), −112.8 (m, CF_2^a), −122.2 (m, CF_2^b), −125.6 (m, CF_2^c), −190.1 (m, CF) ppm. IR (film): ṽ = 3010, 1710, 1680, 1600, 1590, 1510, 1410, 1230, 1140 cm^{-1}. MS: *m*/*z* (%) = 474 (10) [M$^+$], 354, 255, 95. 69.

3-Fluoro-4-(4′-methoxyphenyl)-2-(perfluorobutyl)benzo-1,5-diazepine (6d): ^{1}H NMR: δ = 3.88 (s, O−CH_3), 6.60 (d, $^2J_{H,F}$ = 46.0 Hz, 1 H, 3-H), 7.00 (d, *J* = 7.6 Hz, 2 H, $H_{arom.}$), 7.40 (t, *J* = 7.6 Hz, 1 H, $H_{arom.}$), 7.52 (t, *J* = 7.6 Hz, 1 H, $H_{arom.}$), 7.72 (d, *J* = 7.6 Hz, 2 H, $H_{arom.}$), 7.98 (d, *J* = 7.6 Hz, 1 H, $H_{arom.}$) ppm. ^{13}C NMR: δ = 55.4 (s, O−CH_3), 114.0−131.0 (m, $C_{arom.}$), 138.8 (d, $^1J_{C,F}$ = 270.0 Hz, C-3), 148.7 (m, C-2), 148.7 (m, C-4) ppm. ^{19}F NMR: δ = −81.4 (m, CF_3), −113.1 (m, CF_2^a), −122.3 (m, CF_2^b), −125.6 (m, CF_2^c), −195.5 (m, CF) ppm. IR (film): ṽ = 3010, 2980, 1700, 1670, 1600, 1580, 1510, 1440, 1240, 1140 cm^{-1}. MS: *m*/*z* (%) = 486 (20) [M$^+$], 267, 107. $C_{20}H_{12}F_{10}N_2O$: calcd. C 51.78, H 2.37, N 5.49; found C 51.47, H 2.47, N 5.19.

3-Fluoro-4-pentyl-2-(perfluorobutyl)benzo-1,5-diazepine (6e): ^{1}H NMR: δ = 0.93 (t, *J* = 7.6 Hz, 3 H, CH_3), 1.40 (m, 4 H, 2 CH_2), 1.70−1.95 (m, 2 H, CH_2), 2.60−2.90 (m, 2 H, CH_2), 4.77 (d, $^2J_{H,F}$ = 48.0 Hz, 1 H, 3-H), 7.30−7.65 (m, 4 H, $H_{arom.}$) ppm. ^{13}C NMR: δ = 13.9 (s, CH_3), 22.4 (s, CH_2), 25.7 (s, CH_2), 31.4 (s, CH_2), 33.8 (s, CH_2), 126.1−128.8 (m, $C_{arom.}$), 138.2 (d, $^1J_{C,F}$ = 231.0 Hz, C-3), 142.1 (d, $^2J_{C,F}$ = 24.0 Hz, C-2), 160.5 (d, $^2J_{C,F}$ = 24.0 Hz, C-4) ppm. ^{19}F NMR: δ = −81.5 (m, CF_3), −109.8 (dm, $^1J_{F,F}$ = 295.0 Hz, 1 F, CF_2^a), −112.3 (dm, $^1J_{F,F}$ = 295.0 Hz, 1 F, CF_2^a), −121.6 (m, CF_2^b), −125.5 (m, CF_2^c), −205.8 (m, CF) ppm. IR (film): ṽ = 3590, 3000, 2960, 1620, 1585, 1505, 1450, 1345, 1200, 1130 cm^{-1}. MS: *m*/*z* (%) = 450 (3) [M$^+$], 407 (10), 394 (100), 225 (45), 205 (18), 167 (10). $C_{18}H_{16}F_{10}N_2$: calcd. C 48.01, H 3.58, N 6.22; found C 47.67, H 3.47, N 6.11.

4-(1′-Deoxy-2′,3′:4′,5′-di-*O*-isopropylidene-D-xylityl)-3-fluoro-2-(perfluoroethyl)benzo-1,5-diazepine (6f): Mixture of two diastereomers 50:50. ^{1}H NMR: δ = 1.33−1.46 (m, 12 H, 4 CH_3), 2.85−2.98 (m, 1 H, 1′-H), 3.11−3.21 (m, 1 H, 1′′-H), 3.82−4.04 (m, 3 H, 3′-H, 5′-H, 5′′-H), 4.19−4.36 (m, 1 H, 4′-H), 4.52−4.66 (m, 1 H, 2′-H), 4.81 (d, *J* = 50.8 Hz, 1 H, 3-H one diastereomer), 4.88 (d, *J* = 48.0 Hz, 1 H, 3-H other diastereomer), 7.33−7.56 (m, 4 H, $H_{arom.}$) ppm. ^{13}C NMR: δ = 25.3, 25.3, 26.0, 26.1, 26.8, 26.9, 27.0, 27.1 (s, CH_3), 37.4 (s, C-1′ one dia.), 37.8 (s, C-1′ other dia.), 65.6 (s, C-5′ both dia.), 74.2 (s, C-4′ both dia.), 74.8 (s, C-2′ one dia.), 75.0 (s, C-2′ other diast.), 80.2 (s, C-3′ one dia.), 80.7 (s, C-3′ other dia.), 85.4−85.8 (m, CF_2, CF_3 one diast.), 88.6−89.0 (m, CF_2, CF_3 other dia.), 109.6−109.9 (Cq $_{acet.}$), 126.4−128.8 (m, $C_{arom.}$), 137.8 (d, $^1J_{C,F}$ = 208.7 Hz, C-3 one dia.), 137.9 (d, $^1J_{C,F}$ = 210.7 Hz, C-3 other dia.), 141.6 (d, $^2J_{C,F}$ = 23.6 Hz, C-2 one dia.), 141.7 (d, $^2J_{C,F}$ = 23.6 Hz, C-2 other dia.), 156.5 (d, $^2J_{C,F}$ = 22.6 Hz, C-4 one dia.), 156.6 (d, $^2J_{C,F}$ = 22.6 Hz, C-4 other dia.) ppm. ^{19}F NMR: δ = −81.2 (m, 3 F, CF_3), −113.6 (m, 2 F, CF_2), −206.8 (m, 1 F, CHF) ppm. IR (film): ṽ = 3063, 2989, 2936, 1642, 1599, 1481, 1459, 1372, 770, 735 cm^{-1}.

4-(3′-*O*-Benzyl-5′-deoxy-1′,2′-*O*-isopropylidene-α-D-xylofuranosyl)-3-fluoro-2-(perfluoroethyl)benzo-1,5-diazepine (6g): Mixture of two diastereomers, 50:50. ^{1}H NMR: δ = 1.34 (s, 3 H, CH_3), 1.55 (s, 3 H, CH_3), 3.08 (ddd, $^2J_{5',5''}$ = 16.0, $^3J_{5',4'}$ = 6.9, $^3J_{5',F}$ = 1.9 Hz, 1 H, 5′-H), 3.36 (ddd, $^2J_{5'',5'}$ = 16.0, $^3J_{5'',4'}$ = 6.9, $^3J_{5'',F}$ = 1.5 Hz, 1 H, 5′′-H), 4.12 (d, $^3J_{3',4'}$ = 3.0 Hz, 1 H, 3′-H), 4.37 (d, $^2J_{H,H'}$ =

12.2 Hz, 1 H, H_{benzyl}), 4.52 (d, $^2J_{H,H'}$ = 12.2 Hz, 1 H, H'_{benzyl}), 4.61 (d, $^3J_{2',1'}$ = 3.4 Hz, 1 H, 2′-H), 4.63 (m, $^2J_{H,F}$ = 56.0 Hz, 1 H, 3-H), 4.83 (dt, $^3J_{4',3'}$ = 3.0, $^3J_{4',5'}$ = 6.9, $^3J_{4',5''}$ = 6.9 Hz, 1 H, 4′-H), 5.93 (d, $^3J_{1',2'}$ = 3.4 Hz, 1 H, 1′-H), 7.16−7.57 (m, 9 H, $H_{arom.}$) ppm. ^{13}C NMR: δ = 26.2 (s, CH_3), 26.8 (s, CH_3), 29.7 (s, C-5′), 71.7 (s, CH_2 benzyl), 77.3 (s, C-4′), 81.1 (s, C-3′), 82.3 (s, C-2′), 104.4 (s, C-1′), 111.6 (s, $C_{q,acet.}$), 118.0 (qt, $^1J_{C,F}$ = 287.5, $^2J_{C,F}$ = 35.4 Hz, CF_3), 127.7−128.2−128.3−128.4 ($C_{arom.}$), 136.1−136.2 (s, $C_{q,arom.}$), 137.8 (d, $^2J_{C,F}$ = 210.0 Hz, C-3), 137.8 (d, $^2J_{C,F}$ = 21.7 Hz, C-4) ppm. ^{19}F NMR: δ = −81.4 (m, 3 F, CF_3), −114.0 (d, J = 22.9 Hz, 2 F, CF_2), −206.8 (m, 1 F, CHF) ppm. IR (film): ṽ = 3406, 2928, 2360, 1645, 1457, 1376, 1216, 1076, 757 cm^{-1}. MS: *m*/*z* (%) = 542 (22) [M$^+$], 527 [M − 15], 434, 405, 377, 351, 333, 322, 294 (100), 248. HR MS: calcd. for $C_{26}H_{24}F_6N_2O_4$ 542.1630, found 542.1640.

General Procedure for the Synthesis of Benzothiazepines 7 from 3: The 2-aminothiophenol (4 mmol, 2 equiv.) and $MgSO_4$ were added to a solution of **3** (1 mmol) in diethyl ether (20 mL). The mixture was stirred at reflux for 24 h and washed with an aqueous solution of saturated ammonium chloride. The organic layer was extracted twice with 20 mL of diethyl ether. The organic layer was dried with $MgSO_4$ and filtered, and the diethyl ether was evaporated. Compounds **7a**−**c** were purified by silica gel chromatography (petroleum ether/EtOAc 95:5).

3-Fluoro-4-(4′-fluorophenyl)-2-(perfluorobutyl)benzo-1,5-thiazepine (7a): ^{1}H NMR: δ = 7.15−7.30 (m, 4 H, $H_{arom.}$), 7.40−7.55 (m, 2 H, $H_{arom.}$), 7.90−8.05 (m, 2 H, $H_{arom.}$) ppm. ^{13}C NMR: δ = 116.0 (s, $C_{arom.}$), 125.0 (s, C-2′), 126.0 (s, C-5′), 127.8 (s, C-3′), 130.6 (s, $C_{arom.}$), 131.1 (s, C-6′), 132.7 (s, C-4′), 148.8 (s, C-1′), 153.0 (d, $^1J_{C,F}$ = 301.0 Hz, C-3), 153.6 (m, C-2), 155.4 ($C_{arom.}$), 157.0 (d, $^2J_{C,F}$ = 27.0 Hz, C-4), 165.1 (d, $^1J_{C,F}$ = 253.9 Hz, $CF_{arom.}$) ppm. ^{19}F NMR: δ = −81.4 (m, CF_3), −82.8 (m, CF), −107.4 (m, $CF_{arom.}$), −108.1 (m, CF_2^a), −123.0 (m, CF_2^b), −126.5 (m, CF_2^c) ppm. IR (film): ṽ = 3000, 2960, 1630, 1595, 1570, 1500, 1450, 1410, 1305, 1290, 1240, 1170, 1150, 980 cm^{-1}. $C_{19}H_8F_{11}NS$: calcd. C 46.43, H 1.64, N 2.85; found C 46.75, H 1.53, N 2.66.

4-(1′-Deoxy-2′,3′:4′,5′-di-*O*-isopropylidene-D-xylityl)-3-fluoro-2-(perfluoroethyl)benzo-1,5-thiazepine (7b): ^{1}H NMR: δ = 1.39−1.45 (m, 12 H, 4 CH_3), 3.10−3.55 (m, 2 H, 1′-H, 1′′-H), 3.93 (t, $^2J_{5',5''}$ = $^3J_{5',4'}$ = 8.0 Hz, 1 H, 5′-H), 3.95 (m, 1 H, 3′-H), 4.08 (t, $^2J_{5'',5'}$ = $^3J_{5'',4'}$ = 8.0 Hz, 1 H, 5′′-H), 4.27 (m, 1 H, 4-H), 4.46 (m, 1 H, 2-H), 7.27 (dd, ^3J = 7.6, ^3J = 8.0 Hz, 2 H, $H_{arom.}$), 7.33 (d, J = 8.0 Hz, 1 H, $H_{arom.}$), 7.44 (d, ^3J = 7.6 Hz, 1 H, $H_{arom.}$) ppm. ^{13}C NMR: δ = 25.5 (s, CH_3), 26.1 (s, CH_3), 26.8 (s, CH_3), 27.1 (s, CH_3), 44.0 (s, C-1′), 65.7 (s, C-5′), 74.6 (s, C-4′), 74.8 (s, C-2′), 80.0 (s, C-3′), 109.6 (s, $C_{q\ acet.}$), 109.7 (s, $C_{q\ acet.}$), 126.0 (s, $C_{arom.}$), 128.2 (s, $C_{arom.}$), 130.5 (s, $C_{arom.}$), 132.6 (s, $C_{arom.}$), 148.5 (s, C-2), 153.4 (d, $^1J_{C,F}$ = 298.0 Hz, C-3), 161.0 (d, $^2J_{C,F}$ = 27.6 Hz, C-4) ppm. ^{19}F NMR: δ = −84.5 (m, 3 F, CF_3), −89.4 (m, 1 F, CF), −112.2 (m, 2 F, CF_2) ppm. IR (film): ṽ = 3471, 3368, 2988, 2932, 2360, 1737, 1645, 1458, 1334, 1209, 1066, 751 cm^{-1}. MS: *m*/*z* (%) = 511 (6) [M$^+$], 496 [M − 15], 453, 352, 311, 292, 200 (100), 142, 124. HR MS: calcd. for $C_{22}H_{23}F_6NO_4S$ 511.1249, found 511.1252.

4-(3′-*O*-Benzyl-5′-deoxy-1′,2′-*O*-isopropylidene-α-D-xylofuranosyl)-3-fluoro-2-(perfluoroethyl)benzo-1,5-thiazepine (7c): ^{1}H NMR: δ = 1.26 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3), 3.12−3.47 (m, 2 H, 5′-H, 5′′-H), 4.16 (d, $^3J_{3',4'}$ = 3.0 Hz, 1 H, 3′-H), 4.53 (d, $^2J_{H,H'}$ = 11.8 Hz, 1 H, H-benzyl), 4.64−4.87 (m, 3 H, H′-benzyl, 4′-H, 2′-H), 5.98 (d, $^3J_{1',2'}$ = 3.8 Hz, 1 H, 1′-H), 7.15−7.50 (m, 4 H, $H_{arom.}$) ppm. ^{13}C NMR: δ = 26.3 (s, CH_3), 26.7 (s, CH_3), 29.6 (s, C-5′), 71.8 (s, CH_2 benzyl), 77.5 (s, C-4′), 81.6 (s, C-3′), 82.3 (s, C-2′), 104.6 (s, C-1′), 111.6 (s, $C_{q,acet.}$), 118.0 (qt, $^1J_{C,F}$ = 287.4, $^2J_{C,F}$ = 35.4 Hz, CF_3), 125.4−132.5 (m, $CH_{arom.}$), 137.3 (s, $C_{q,arom.}$), 148.5 (s, C-2), 153.3 (d, $^1J_{C,F}$ = 305.0 Hz, C-3), 160.2 (d, $^2J_{C,F}$ = 27.6 Hz, C-4) ppm. ^{19}F NMR: δ = −84.5 (m, 3 F, CF_3), −90.2 (dm, $^4J_{F,F}$ = 26.7 Hz, 1 F, CF), −112.1 (d, $^4J_{F,F}$ = 26.7 Hz, 2 F, CF_2). IR (film): ṽ = 3375, 2931, 2360, 1723, 1645, 1456, 1375, 1219, 1077, 1028, 753 cm^{-1}. MS: *m*/*z* (%) = 559 (19) [M$^+$], 544 [M − 15], 451, 368, 351, 311 (100). HR MS: calcd. for $C_{26}H_{23}F_6NO_4S$ 559.1245, found 559.1252.

3-Fluoro-2-(4′-fluorophenyl)-4-(perfluorobutyl)quinoline (8a): The benzothiazepine **7a** (0.2 g, 0.41 mmol) was heated at reflux and stirred for 12 h in toluene in a round-bottomed flask. After evaporation of the toluene, the crude product was purified by flash chromatography (eluent: petroleum ether/dichloromethane, 70:30) to give pure **8a** (0.14 g, 80%). ^{1}H NMR: δ = 7.15−7.30 (m, 2 H, $H_{arom.}$), 7.65 (t, J = 7.6 Hz, 1 H, $H_{arom.}$), 7.75 (t, J = 7.6 Hz, 1 H, $H_{arom.}$), 8.05 (m, 2 H, $H_{arom.}$), 8.20 (t, J = 7.6 Hz, 2 H, $H_{arom.}$) ppm. ^{13}C NMR: δ = 115.0−132.0 (11 $C_{arom.}$), 145.4 (s, C-1′), 148.5 (d, $^2J_{C,F}$ = 18.0 Hz, C-2), 153.2 (d, $^1J_{C,F}$ = 275.0, C-3), 154.4 (m, C-4), 164.0 (d, $^1J_{C,F}$ = 252.0 Hz, C-4′) ppm. ^{19}F NMR: δ = −81.4 (m, CF_3), −104.3 (m, CF_2^a), −110.8 (m, $CF_{arom.}$), −119.1 (tt, J = 39.1 Hz, CF), −122.0 (m, CF_2^b), −126.4 (m, CF_2^c) ppm. IR (film): ṽ = 3010, 1590, 1630, 1550, 1500, 1450, 1360, 1220, 1110, 1020 cm^{-1}. MS: *m*/*z* (%) = 459 (10) [M$^+$], 440, 364, 240, 219, 95. $C_{19}H_8F_{11}N$: calcd. C 49.69, H 1.76, N 3.05; found C 49.69, H 1.64, N 3.00.

General Procedure for the Synthesis of Pyrimidines 9 from 3: The amidinium salt (5 mmol, 5 equiv.) was stirred with KOH (3 mmol, 3 equiv.) for 1 h in dichloromethane (10 mL), and a solution of **3** (1 mmol) in dichloromethane (5 mL) was added. The mixture was stirred at room temperature for 24 h and then washed with a saturated solution of ammonium chloride. The aqueous layer was extracted twice with diethyl ether. The organic layer was dried with $MgSO_4$ and filtered. After solvent removal, compounds **9b**−**i** were purified by silica gel chromatography (petroleum ether/EtOAc, 95:5 or 90:10).

5-Fluoro-6-(4′-fluorophenyl)-4-(perfluorobutyl)pyrimidine (9a): ^{1}H NMR: δ = 7.25 (m, 2 H, $H_{arom.}$), 8.22 (m, 2 H, $H_{arom.}$), 9.17 (s, 1 H, H-2) ppm. ^{13}C NMR: δ = 105.0−120.0 (m, C_4F_9), 116.1 (s, $C_{arom.}$), 128.1 (s, C-2), 131.9 (s, $C_{arom.}$), 143.2 (m, $CF_{arom.}$), 153.6 (s, $C_{arom.}$), 153.8 (d, $^1J_{C,F}$ = 281.0 Hz, C-5), 154.4 (d, $^2J_{C,F}$ = 9.0 Hz, C-4), 165.1 (d, $^1J_{C,F}$ = 255.0 Hz, $CF_{arom.}$) ppm. ^{19}F NMR: δ = −81.4 (t, $^3J_{F,F}$ = 9.0 Hz, CF_3), −106.9 (m, $CF_{arom.}$), −114.2 (m, CF_2^a), −123.3 (m, CF_2^b), −126.3 (m, CF_2^c), −131.7 (m, CF) ppm. IR (film): ṽ = 3000, 1600, 1580, 1500, 1420, 1400, 1360, 1300, 1240, 1170, 1150, 1010 cm^{-1}. MS: *m*/*z* (%) = 411 (19) [M + 1], 411 (97) [M$^+$], 391, 241 (100), 164, 69. $C_{14}H_5F_{11}N_2$: calcd. C 40.99, H 1.23, N 6.83; found C 41.21, H 1.15, N 6.55.

6-(1′-Deoxy-2′,3′;4′,5′-di-*O*-isopropylidene-D-xylityl)-5-fluoro-4-(perfluoroethyl)pyrimidine (9b): ^{1}H NMR: δ = 1.25 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3), 1.37 (s, 3 H, CH_3), 1.43 (s, 3 H, CH_3), 3.23 (ddd, $^2J_{1',1''}$ = 14.1, $^3J_{1',2'}$ = 4.2, $^4J_{1',F}$ = 2.3 Hz, 1 H, 1′-H), 3.26 (ddd, $^2J_{1'',1'}$ = 14.1, $^3J_{1'',2'}$ = 7.6, $^4J_{1'',F}$ = 2.3 Hz, 1 H, 1′′-H), 3.90 (dd, $^2J_{5',5''}$ = 8.0, $^3J_{5',4'}$ = 4.6 Hz, 1 H, 5′-H), 4.01 (dd, $^3J_{3',2'}$ = 7.6, $^3J_{3',4'}$ = 4.6 Hz, 1 H, 3′-H), 4.13 (dd, $^2J_{5'',5'}$ = 8.0, $^3J_{5'',4'}$ = 6.9 Hz, 1 H, 5′′-H), 4.28 (dt, $^3J_{4',5'}$ = 6.9, $^3J_{4',3'}$ = 4.6 Hz, 1 H, 4′-H), 4.51 (dt, $^3J_{2',3'}$ = 7.6, $^3J_{2',\ 1''}$ = 7.6, $^3J_{2',1'}$ = 4.2 Hz, 1 H, 2′-H), 9.09 (s, 1 H, $H_{pyrimidine}$) ppm. ^{13}C NMR: δ = 25.1 (s, CH_3), 26.0 (s, CH_3), 26.8 (s, CH_3), 26.9 (s, CH_3), 35.3 (s, C-1′), 65.5 (s, C-5′), 74.5 (s, C-4′), 74.8 (s, C-2′), 79.8 (s, C-3′), 109.9 (s, $C_{q,acet.}$), 110.1 (s, $C_{q,acet.}$), 118.4 (dt, $^1J_{C,F}$ = 287.4, $^2J_{C,F}$ = 35.4 Hz, CF_3), 153.4 (s, C-6), 153.5 (s, C-2), 154.7 (d, $^1J_{C,F}$ = 279.6 Hz; C-5), 158.7 (d,

$^2J_{C,F}$ = 15.7 Hz, C-4) ppm. ^{19}F NMR: δ = −83.6 (m, 3 F, CF_3), −117.4 (d, $^4J_{F,F}$ = 22.9 Hz, 2 F, CF_2), −131.9 (t, $^4J_{F,F}$ = 22.9 Hz, 1 F, CF) ppm. IR (film): ṽ = 3523, 2988, 2936, 2360, 1735, 1590, 1457, 1334, 1217, 1075, 744 cm^{-1}. MS: *m*/*z* (%) = 431 (43) [M + 1], 415 (100) [M − 15], 329, 297, 271, 143. HR MS: calcd. for $C_{17}H_{20}F_6N_2O_4$ 430.1408; found 430.1405.

6-(1′-Deoxy-2′,3′;4′,5′-di-*O*-isopropylidene-D-xylityl)-5-fluoro-2-methyl-4-(perfluoroethyl)pyrimidine (9c): ^{1}H NMR: δ = 1.25 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3), 1.44 (s, 3 H, CH_3), 2.76 (s, 3 H, CH_3 pyrimidine), 3.10 (ddd, $^2J_{1′,1″}$ = 14.1, $^3J_{1′,2′}$ = 3.8, $^4J_{1′,F}$ = 1.9 Hz, 1 H, 1′-H), 3.23 (ddd, $^2J_{1″,1′}$ = 14.1, $^3J_{1″,2′}$ = 8.0, $^4J_{1″,F}$ = 1.9 Hz, 1 H, 1″-H), 3.90 (dd, $^2J_{5′,5″}$ = 8.4, $^3J_{5′,4′}$ = 7.6 Hz, 1 H, 5′-H), 3.99 (dd, $^3J_{3′,2′}$ = 7.6, $^3J_{3′,4′}$ = 4.6 Hz, 1 H, 3′-H), 4.09 (dd, $^2J_{5″,5′}$ = 8.4, $^3J_{5″,4′}$ = 6.9 Hz, 1 H, 5″-H), 4.26 (ddd, $^3J_{4′,5′}$ = 7.6, $^3J_{4′,5″}$ = 6.9, $^3J_{4′,3′}$ = 4.6 Hz, 1 H, 4′-H), 4.48 (dt, $^3J_{2′,\ 1″}$ = 8.0, $^3J_{2′,3′}$ = 7.6, $^3J_{2′,1′}$ = 3.8 Hz, 1 H, 2′-H) ppm. ^{13}C NMR: δ = 25.1 (s, CH_3), 25.2 (s, CH_3 pyrimidine), 26.0 (s, CH_3), 26.9 (s, CH_3), 26.9 (s, CH_3), 35.4 (s, C-1′), 65.5 (s, C-5′), 74.7 (s, C-4′), 75.0 (s, C-2′), 80.0 (s, C-3′), 109.8 (s, $C_{q,acet.}$), 110.0 (s, $C_{q,acet.}$), 118.3 (qt, $^1J_{C,F}$ = 287.3, $^2J_{C,F}$ = 35.1 Hz, CF_3), 153.2 (d, $^1J_{C,F}$ = 273.7 Hz, C-5), 157.9 (s, C-6), 158.2 (s, C-2), 163.5 (d, $^2J_{C,F}$ = 9.8 Hz, C-4) ppm. ^{19}F NMR: δ = −83.6 (m, 3 F, CF_3), −117.6 (d, $^4J_{F,F}$ = 19.1 Hz, 2 F, CF_2), −139.2 (t, $^4J_{F,F}$ = 19.1 Hz, 1 F, CF) ppm. IR (film): ṽ = 3421, 2989, 2933, 2360, 1731, 1587, 1430, 1334, 1168, 1210, 1075, 737 cm^{-1}. MS: *m*/*z* (%) = 445 (30) [M + 1], 429 (100) [M − 15], 386, 369, 343, 311, 285. HR MS: calcd. for $C_{18}H_{23}F_6N_2O_4$ 445.1534; found 445.1562.

6-(1′-Deoxy-2′,3′;4′,5′-di-*O*-isopropylidene-D-xylityl)-5-fluoro-2-methoxy-4-(perfluoroethyl)pyrimidine (9d): ^{1}H NMR: δ = 1.35−1.37 (s, 9 H, 3 CH_3), 1.43 (s, 3 H, CH_3), 3.05 (ddd, $^2J_{1′,1″}$ = 14.1, $^3J_{1′,2′}$ = 3.1, $^4J_{1′,F}$ = 2.3 Hz, 1 H, 1′-H), 3.21 (ddd, $^2J_{1″,1′}$ = 14.1, $^3J_{1″,2′}$ = 8.0, $^4J_{1″,F}$ = 1.6 Hz, 1 H, 1″-H), 3.91 (dd, $^2J_{5′,5″}$ = 8.4, $^3J_{5′,4′}$ = 7.6 Hz, 1 H, 5′-H), 3.98 (dd, $^3J_{3′,2′}$ = 8.0, $^3J_{3′,4′}$ = 4.6 Hz, 1 H, 3′-H), 4.00 (s, 3 H, O−CH_3), 4.06 (dd, $^2J_{5″,5′}$ = 8.4, $^3J_{5″,4′}$ = 7.6 Hz, 1 H, 5″-H), 4.29 (dt, $^3J_{4′,5′}$ = 7.6, $^3J_{4′,5″}$ = 7.6, $^3J_{4′,3′}$ = 4.6 Hz, 1 H, 4′-H), 4.49 (dt, $^3J_{2′,3′}$ = 8.0, $^3J_{2′,\ 1″}$ = 8.0, $^3J_{2′,1′}$ = 3.1 Hz, 1 H, 2′-H) ppm. ^{13}C NMR: δ = 25.1 (s, CH_3), 26.0 (s, CH_3), 26.9 (s, CH_3), 26.9 (s, CH_3), 35.7 (s, C-1′), 55.9 (s, O−CH_3), 65.4 (s, C-5′), 74.6 (s, C-4′), 74.8 (s, C-2′), 80.0 (s, C-3′), 109.7 (s, $C_{q,acet.}$), 110.0 (s, $C_{q,acet.}$), 118.0 (qt, $^1J_{C,F}$ = 286.9, $^2J_{C,F}$ = 35.9 Hz, CF_3), 150.8 (d, $^1J_{C,F}$ = 264.8 Hz, C-5), 160.1 (s, C-6), 160.2 (s, C-2), 161.6 (d, $^2J_{C,F}$ = 16.7 Hz, C-4) ppm. ^{19}F NMR: δ = −83.5 (m, 3 F, CF_3), −117.6 (dd, $^4J_{F,F}$ = 19.1 Hz, 2 F, CF_2), −143.2 (t, $^4J_{F,F}$ = 19.1 Hz, 1 F, CF) ppm. IR (film): ṽ = 3503, 2988, 2935, 2360, 1734, 1585, 1474, 1334, 1213, 1076, 744 cm^{-1}. MS: *m*/*z* (%) = 461 (100) [M + 1], 445 [M − 15], 427, 403, 385, 327, 201, 143. HR MS: calcd. for $C_{18}H_{23}F_6N_2O_4$ 445.1534; found 445.1562.

2-Amino-6-(1′-deoxy-2′,3′;4′,5′-di-*O*-isopropylidene-D-xylityl)-5-fluoro-4-(perfluoroethyl)pyrimidine (9e): ^{1}H NMR: δ = 1.26 (s, 3 H, CH_3), 1.39 (s, 3 H, CH_3), 1.41 (s, 3 H, CH_3), 1.46 (s, 3 H, CH_3), 2.96 (ddd, $^2J_{1′,1″}$ = 14.1, $^3J_{1′,2′}$ = 4.2, $^4J_{1′,F}$ = 2.3 Hz, 1 H, 1′-H), 3.11 (ddd, $^2J_{1″,1′}$ = 14.1, $^3J_{1″,2′}$ = 7.6, $^4J_{1″,F}$ = 2.3 Hz, 1 H, 1″-H), 3.91 (dd, $^2J_{5′,5″}$ = 8.0, $^3J_{5′,4′}$ = 6.9 Hz, 1 H, 5′-H), 3.96 (dd, $^3J_{3′,2′}$ = 7.6, $^3J_{3′,4′}$ = 4.2 Hz, 1 H, 3′-H), 4.09 (dd, $^2J_{5″,5′}$ = 8.0, $^3J_{5″,4′}$ = 6.5 Hz, 1 H, 5″H), 4.23 (dt, $^3J_{4′,5′}$ = 6.9, $^3J_{4′,5″}$ = 6.5, $^3J_{4′,3′}$ = 4.2 Hz, 1 H, 4′-H), 4.45 (dt, $^3J_{2′,3′}$ = 7.6, $^3J_{2′,\ 1″}$ = 7.6, $^3J_{2′,1′}$ = 4.2 Hz, 1 H, 2′-H), 5.30 (s, 2 H, NH_2) ppm. ^{13}C NMR: δ = 25.0 (s, CH_3), 26.1 (s, CH_3), 27.0 (s, CH_3), 27.1 (s, CH_3), 35.8 (s, C-1′), 65.5 (s, C-5′), 74.3 (s, C-4′), 75.0 (s, C-2′), 80.2 (s, C-3′), 110.0 (s, $C_{q,acet.}$), 110.2 (s, $C_{q,acet.}$), 118.5 (qt, $^1J_{C,F}$ = 287.7, $^2J_{C,F}$ = 36.1 Hz, CF_3), 150.8 (d, $^1J_{C,F}$ = 265.9 Hz, C-5), 158.2 (s, C-6), 160.0 (s, C-2), 160.4 (s, C-4) ppm. ^{19}F NMR: δ = −83.7 (m, 3 F, CF_3), −118.2 (d, $^4J_{F,F}$ = 19.1 Hz, 2 F, CF_2), −151.1 (tm, $^4J_{F,F}$ = 19.1 Hz, 1 F, CF) ppm. IR (film): ṽ = 3503, 2988, 2935, 2360, 1734, 1585, 1474, 1334, 1213, 1076, 744 cm^{-1}. MS: *m*/*z* (%) = 430 [M − 15], 376, 312, 246, 185, 156.

6-(3′-*O*-Benzyl-5′-deoxy-1′,2′-*O*-isopropylidene-α-D-xylofuranosyl)-5-fluoro-4-(perfluoroethyl)pyrimidine (9f, major diastereomer): ^{1}H NMR: δ = 1.35 (s, 3 H, CH_3), 1.51 (s, 3 H, CH_3), 3.12 (ddd, $^2J_{5′,5″}$ = 16.0, $^3J_{5′,4′}$ = 6.9, $^3J_{5′,F}$ = 1.9 Hz, 1 H, 5-H), 3.43 (ddd, $^2J_{5″,5′}$ = 16.0, $^3J_{5″,4′}$ = 6.9, $^3J_{5″,F}$ = 1.9 Hz, 1 H, 5″-H), 4.07 (d, $^3J_{3′,4′}$ = 3.1 Hz, 1 H, 3′-H), 4.39 (d, $^2J_{H,H′}$ = 11.9 Hz, 1 H, H_{benzyl}), 4.69 (d, $^3J_{2′,1′}$ = 3.8 Hz, 1 H, 2′-H), 4.70 (d, $^2J_{H,H′}$ = 11.9 Hz, 1 H, $H′_{benzyl}$), 4.81 (dt, 1 H, $^3J_{4′,5′}$ = 6.9, $^3J_{4′,5′}$ = 6.9, $^3J_{4′,3′}$ = 3.1 Hz, 4′-H), 5.96 (d, $^3J_{1′,2′}$ = 3.8 Hz, 1 H, 1′-H), 7.19−7.35 (m, 5 H, $H_{arom.}$), 8.90 (s, 1 H, 8-H) ppm. ^{13}C NMR: δ = 26.2 (s, CH_3), 26.7 (s, CH_3), 29.6 (s, C-5′), 71.6 (s, CH_2 benzyl), 77.5 (s, C-4′), 81.3 (s, C-3′), 82.2 (s, C-2′), 104.7 (s, C-1′), 111.7 (s, $C_{q,acet.}$), 118.0 (qt, $^1J_{C,F}$ = 287.5, $^2J_{C,F}$ = 35.4 Hz, CF_3), 127.9−128.1−128.4 (m, $CH_{arom.}$), 136.9 (s, $C_{q,arom.}$), 153.2 (s, C-6), 153.3 (s, C-2), 154.2 (d, $^1J_{C,F}$ = 279.6 Hz, C-5), 159.2 (d, $^2J_{C,F}$ = 13.8 Hz, C-4) ppm. ^{19}F NMR: δ = −83.5 (m, 3 F, CF_3), −117.3 (d, $^4J_{F,F}$ = 19.1 Hz, 2 F, CF_2), −131.9 (t, $^4J_{F,F}$ = 19.1 Hz, 1 F, CF) ppm. IR (film): ṽ = 3262, 2990, 2256, 1726, 1591, 1415, 1332, 1215, 1072, 1022, 733 cm^{-1}. MS: *m*/*z* (%) = 479 (66) [M$^+$], 461, 421, 341, 313 (100).

6-(3′-*O*-Benzyl-5′-deoxy-1′,2′-*O*-isopropylidene-β-L-arabinofuranosyl)-5-fluoro-4-(perfluoroethyl)pyrimidine (9f, minor diastereomer): ^{1}H NMR: δ = 4.02 (d, $^3J_{3′,4′}$ = 2.1 Hz, 1 H, 3′-H), 5.93 (d, $^3J_{1′,2′}$ = 4.2 Hz, 1 H, 1′-H), 9.04 (s, 1 H, 8-H) ppm. ^{19}F NMR: δ = −132.4 (t, $^4J_{F,F}$ = 19.1 Hz, 1 F, CF) ppm.

6-(3′-*O*-Benzyl-5′-deoxy-1′,2′-*O*-isopropylidene-α-D-xylofuranosyl)-5-fluoro-2-methyl-4-(perfluoroethyl)pyrimidine (9g, major diastereomer): ^{1}H NMR: δ = 1.34 (s, 3 H, CH_3), 1.51 (s, 3 H, CH_3), 2.63 (s, 3 H, CH_3 pyrimidine), 2.96 (ddd, $^2J_{5′,5″}$ = 16.0, $^3J_{5′,4′}$ = 6.9, $^3J_{5′,F}$ = 1.9 Hz, 1 H, 5′-H), 3.39 (ddd, $^2J_{5″,5′}$ = 16.0, $^3J_{5″,4′}$ = 7.2, $^3J_{5″,F}$ = 1.5 Hz, 1 H, 5″-H), 4.04 (d, $^3J_{3′,4′}$ = 3.4 Hz, 1 H, 3′-H), 4.40 (d, $^2J_{H,H′}$ = 12.2 Hz, 1 H, H_{benzyl}), 4.70 (d, $^3J_{2′,1′}$ = 3.8 Hz, 1 H, 2′-H), 4.72 (d, $^2J_{H,H′}$ = 12.2 Hz, 1 H, $H′_{benzyl}$), 4.77 (dt, $^3J_{4′,5′}$ = 6.9, $^3J_{4′,5″}$ = 6.9, $^3J_{4′,3′}$ = 3.4 Hz, 1 H, 4′-H), 5.95 (d, $^3J_{1′,2′}$ = 3.8 Hz, 1 H, 1′-H), 7.18−7.28 (m, 5 H, $H_{arom.}$) ppm. ^{13}C NMR: δ = 25.2 (s, CH_3 pyrimidine), 26.3 (s, CH_3), 26.8 (s, CH_3), 29.7 (s, C-5′), 71.6 (s, CH_2 benzyl), 77.9 (s, C-4′), 81.3 (s, C-3′), 82.3 (s, C-2′), 104.8 (s, C-1′), 111.8 (s, $C_{q,acet.}$), 118.8 (qt, $^1J_{C,F}$ = 285.5, $^2J_{C,F}$ = 35.4 Hz, CF_3), 127.9−128.1−128.4 ($CH_{arom.}$), 137.1 ($C_{q,arom.}$), 152.7 (d, $^1J_{C,F}$ = 265.8 Hz, C-5), 158.6 (s, C-6), 158.8 (s, C-2), 163.5 (s, C-4) ppm. ^{19}F NMR: δ = −83.6 (m, 3 F, CF_3), −117.5 (d, $^4J_{F,F}$ = 19.1 Hz, 2 F, CF_2), −139.3 (t, $^4J_{F,F}$ = 19.1 Hz, 1 F, CF) ppm. IR (film): ṽ = 3439, 2978, 2360, 1730, 1587, 1429, 1339, 1336, 1211, 1068, 1026, 734 cm^{-1}. MS: *m*/*z* (%) = 493 (92) [M + 1], 477, 435, 355, 244 (100). HR MS: calcd. for $C_{22}H_{22}F_6N_2O_4$ 492.1490, found 492.1483.

6-(3′-*O*-Benzyl-5′-deoxy-1′,2′-*O*-isopropylidene-β-L-arabinofuranosyl)-5-fluoro-2-methyl-4-(perfluoroethyl)pyrimidine (9g, minor diastereomer): ^{1}H NMR: δ = 2.64 (s, 3 H, CH_3 pyrimidine), 4.02 (d, $^3J_{3′,4′}$ = 2.3 Hz, 1 H, 3′-H), 5.91 (d, $^3J_{1′,2′}$ = 4.2 Hz, 1 H, 1′-H) ppm. ^{19}F NMR: δ = −139.7 (t, $^4J_{F,F}$ = 19.1 Hz, 1 F, CF) ppm.

6-(3′-*O*-Benzyl-5-deoxy-1′,2′-*O*-isopropylidene-α-D-xylofuranosyl)-5-fluoro-2-methoxy-4-(perfluoroethyl)pyrimidine (9h, major diastereomer): ^{1}H NMR: δ = 1.34 (s, 3 H, CH_3), 1.50 (s, 3 H, CH_3), 3.14 (ddd, $^2J_{5′,5″}$ = 16.0, $^3J_{5′,4′}$ = 6.9, $^3J_{5′,F}$ = 1.9 Hz, 1 H, 5′-H), 3.39 (ddd, $^2J_{5″,5′}$ = 16.0, $^3J_{5″,4′}$ = 6.9, $^3J_{5′,F}$ = 1.1 Hz, 1 H, 5″-H), 3.92 (s, 3 H, O−CH_3), 4.05 (d, $^3J_{3′,4′}$ = 3.4 Hz, 1 H, 3′-H),

4.40 (d, $^2J_{H,H'}$ = 12.2 Hz, 1 H, H_{benzyl}), 4.68 (d, $^3J_{2',1'}$ = 3.8 Hz, 1 H, 2′-H), 4.70 (d, $^2J_{H,H'}$ = 12.2 Hz, 1 H, H'_{benzyl}), 4.83 (dt, $^3J_{4',5'}$ = 6.9, $^3J_{4',5''}$ = 6.9, $^3J_{4',3'}$ = 3.4 Hz, 1 H, 4′-H), 5.95 (d, $^3J_{1',2'}$ = 3.8 Hz, 1 H, 1′-H), 7.17−7.27 (m, 5 H, $H_{arom.}$) ppm. ^{13}C NMR: δ = 26.3 (s, CH_3), 26.8 (s, CH_3), 29.8 (s, C-5′), 55.7 (s, O−CH_3), 71.6 (s, CH_2 benzyl), 77.7 (s, C-4′), 81.3 (s, C-3′), 82.3 (s, C-2′), 104.7 (s, C-1′), 111.7 (s, $C_{q,acet.}$), 118.8 (qt, $^1J_{C,F}$ = 287.5, $^2J_{C,F}$ = 35.4 Hz, CF_3), 127.9−128.0−128.4 (m, $CH_{arom.}$), 137.0 ($C_{q,arom.}$), 150.3 (d, $^1J_{C,F}$ = 265.8 Hz, C-5), 152.5 (s, C-6), 160.0 (s, C-2), 161.8 (s, C-4) ppm. ^{19}F NMR: δ = −83.4 (m, 3 F, CF_3), −117.5 (d, $^4J_{F,F}$ = 22.9 Hz, 2 F, CF_2), −146.1 (t, $^4J_{F,F}$ = 22.9 Hz, 1 F, CF) ppm. IR (film): ṽ = 3417, 2926, 2856, 1733, 1586, 1415, 1333, 1215, 1076, 1029, 759 cm^{-1}. MS: *m/z* (%) = 508 (5) [M$^+$], 493 [M − 15], 371, 343, 315, 299, 273, 260 (100). HR MS: calcd. for $C_{22}H_{22}F_6N_2O_5$ 508.1435, found 508.1433.

6-(3′-*O*-Benzyl-5-deoxy-1′,2′-*O*-isopropylidene-β-L-arabinofuranosyl)-5-fluoro-2-methoxy-4-(perfluoroethyl)pyrimidine (9h, minor diastereomer): ^{1}H NMR: δ = 3.40 (s, 3 H, OCH_3), 5.92 (d, $^3J_{1',2'}$ = 4.2 Hz, 1 H, 1′-H) ppm. ^{19}F NMR: δ = −146.6 (tm, $^4J_{F,F}$ = 22.0 Hz, 1 F, CF) ppm.

2-Amino-6-(3′-*O*-benzyl-5-deoxy-1′,2′-*O*-isopropylidene-α-D-xylofuranosyl)-5-fluoro-4-(perfluoroethyl)pyrimidine (9i, major diastereomer): ^{1}H NMR: δ = 1.34 (s, 3 H, CH_3), 1.50 (s, 3 H, CH_3), 3.09 (ddd, $^2J_{5',5''}$ = 16.0, $^3J_{5',4'}$ = 6.9, $^3J_{5',F'}$ = 1.9 Hz, 1 H, 5′-H), 3.24 (ddd, $^2J_{5'',5'}$ = 16.0, $^3J_{5'',4'}$ = 6.9, $^3J_{5'',F}$ = 1.1 Hz, 1 H, 5′′-H), 4.01 (d, $^3J_{3',4'}$ = 3.0 Hz, 1 H, 3′-H), 4.41 (d, $^2J_{H,H'}$ = 11.8 Hz, 1 H, H_{benzyl}), 4.71 (d, $^3J_{2',1'}$ = 3.8 Hz, 1 H, 2′-H), 4.77 (d, $^2J_{H,H'}$ = 11.8 Hz, 1 H, H'_{benzyl}), 5.08 (s, 2 H, NH_2), 5.10 (dt, 1 H, $^3J_{4',5'}$ = 6.9, $^3J_{4',5''}$ = 6.9, $^3J_{4',3'}$ = 3.0 Hz, 4′-H), 5.96 (d, $^3J_{1',2'}$ = 3.8 Hz, 1 H, 1′-H), 7.21−7.35 (m, 5 H, $H_{arom.}$) ppm. ^{13}C NMR: δ = 26.1 (s, CH_3), 26.7 (s, CH_3), 29.6 (s, C-5′), 71.6 (s, CH_2 benzyl), 77.6 (s, C-4′), 81.2 (s, C-3′), 82.1 (s, C-2′), 104.7 (s, C-1′), 111.6 (s, $C_{q,acet.}$), 118.5 (qt, $^1J_{C,F}$ = 287.4, $^2J_{C,F}$ = 35.1 Hz, CF_3), 127.8−128.0−128.4 (m, $CH_{arom.}$), 140.2 (s, $C_{q,arom.}$), 148.3 (d, $^1J_{C,F}$ = 265.8 Hz, C-5), 158.3 (s, C-6), 160.1 (s, C-2), 160.3 (s, C-4) ppm. ^{19}F NMR: δ = −83.7 (m, 3 F, CF_3), −118.2 (d, $^4J_{F,F}$ = 22.9 Hz, 2 F, CF_2), −151.4 (t, $^4J_{F,F}$ = 22.9 Hz, 1 F, CF) ppm. IR (film): ṽ = 3354, 3224, 2928, 2856, 2360, 1729, 1621, 1464, 1333, 1216, 1075, 1028, 758 cm^{-1}. MS: *m/z* (%) = 493 (83) [M$^+$], 478 [M − 15], 356, 328, 284, 258, 245 (100), 129. HR MS: calcd. for $C_{21}H_{21}F_6N_3O_4$ 493.1446; found 493.1436.

2-Amino-6-(3′-*O*-benzyl-5-deoxy-1′,2′-*O*-isopropylidene-β-L-arabinofuranosyl)-5-fluoro-4-(perfluoroethyl)pyrimidine (9i minor diastereomer): ^{1}H NMR: δ = 5.34 (s, 2 H, NH_2), 5.93 (d, $^3J_{1',2'}$ = 4.2 Hz, 1 H, 1′-H) ppm. ^{19}F NMR: δ = −151.9 (t, $^4J_{F,F}$ = 22.9 Hz, 1 F, CF) ppm.

Acknowledgments

The authors thank the "Ministère de l'Education Nationale, de l'Enseignement Supérieur et de la Recherche" for doctoral fellowships (F. C., P. D.), and H. Baillia (NMR) and S. Lanthony (HPLC) for their technical assistance. They also thank the ATOFINA company for the generous gift of perfluoroalkyl iodides.

[1] [1a] J. F. Liebman, A. Greenberg, W. R. Dolbier, *Fluorine-Containing Molecules, Structure, Reactivity, Synthesis and Application*, VCH Publishers, New York, **1988**. [1b] J. T. Welch, *Tetrahedron* **1987**, *43*, 3123−3197. [1c] R. Filler, Y. Kobayashi, *Biomedicinal Aspects of Fluorine Chemistry*, Kodansha and Elsevier Biomedical, Tokyo and New York, **1982**.

[2] [2a] *Biomedical Frontiers of Fluorine Chemistry* (Eds. I. Ojima, J. R. McCarthy, J. T. Welch); A.C.S. Editions, Washington, DC, **1996**. [2b] *Organofluorine Chemistry; Principles and Commercial Applications* (Eds.: R. E. Banks, B. E. Smart, J. C. Tatlow); Plenum Press, New York, **1994**. [2c] *Organofluorine Compounds in Medicinal and Biochemical Applications* (Eds.: R. Filler, Y. Kobayashi, L. N. Yagupolskii); Elsevier, Amsterdam, **1993**.

[3] *The Chemistry of Heterocycles.* (Eds.: T. Eicher, S. Hauptmann), Georg Thieme Verlag, Stuttgart, **1995**. *Comprehensive Heterocyclic Chemistry II.* (Eds.: A.R. Katritzky, C. W. Rees, E. F. V. Scriven), Elsevier, Oxford, UK, **1996**.

[4] [4a] E. De Clercq, *Intervirology* **1997**, *40*, 295. [4b] E. De Clercq, *Nucleosides Nucleotides* **1994**, *13*, 1271. [4c] N. G. Johansson, *Adv. Antivir. Drug Design* **1993**, *1*, 87. [4d] C. K. Chu, S. J. Cutler, *J. Heterocycl. Chem.* **1986**, *23*, 289.

[5] [5a] For monofluoration, see: S. D. Taylor, C. C. Kotoris, G. Hum, *Tetrahedron* **1999**, *55*, 12431−12477. [5b] For trifluoromethylation, see: R. P. Singh, J. M. Shreeve, *Tetrahedron* **2000**, *56*, 7613−7632. M. A. McClinton, D. A. McClinton, *Tetrahedron* **1992**, *48*, 6555−6666. [5c] For perfluoroalkylation, see: G. K. S. Prakash, A. K. Yudin, *Chem. Rev.* **1997**, *97*, 757−786. D. J. Burton, Z.-I. Yang, *Tetrahedron* **1992**, *48*, 189−275.

[6] K. Burger, U. Wucherpfennig, E. Brunner, *Adv. Heterocycl. Chem.* **1994**, *60*, 1, and references cited therein.

[7] J.-P. Bouillon, Z. Janousek, H. G. Viehe, *Synth. Commun.* **1995**, *25*, 3961−3971.

[8] K. Funabiki, K. Tamura, T. Ishihara, H. Yamanaka, *Bull. Chem. Soc. Jpn.* **1994**, *67*, 3021−3029.

[9] V. Y. Sosnovskikh, V. A. Kutsenko, *Russ. Chem. Bull.* **1999**, *48*, 540−551.

[10] V. I. Saloutin, Z. E. Skryabina, Y. V. Burgart, *J. Fluorine Chem.* **1992**, *56*, 325−334.

[11] R. E. Pastor, C. A. Giovannoni, A. R. Cambon, *Eur. J. Med. Chem.* **1974**, *9*, 175−176.

[12] M. Ohkoshi, M. Yoshida, H. Matsumaya, M. Iyoda, *Tetrahedron Lett.* **2001**, *42*, 33−36.

[13] [13a] O. G. Kuzueva, Y. V. Burgart, V. I. Saloutin, O. N. Chupakhin, *Chem. Heterocycl. Comp.* **2001**, *37*, 1130−1135. [13b] D. V. Sevenard, O. G. Khomutov, O. V. Koryakova, V. V. Sattarova, M. I. Kodess, J. Stelten, I. Loop, E. Lork, K. I. Pashkevich, G. V. Roschenthaler, *Synthesis* **2000**, 1738−1748. [13c] A. Kreutzberger, A. Burger, *J. Fluorine Chem.* **1993**, *60*, 257−261. [13d] H. Berber, M. Soufyane, C. Mirand, S. Schmidt, A.-M. Aubertin, *Tetrahedron* **2001**, *57*, 7369−7375.

[14] H.-B. Yu, W.-Y. Huang, *J. Fluorine Chem.* **1997**, *84*, 65−67.

[15] K. Funabiki, H. Nakamura, M. Matsui, K. Shibata, *Synlett* **1999**, 756−758.

[16] [16a] B.-H. Luo, H.-P. Guan, C.-M. Hu, *Synlett* **1997**, 1261−1262. [16b] H.-P. Guan, Q.-S. Hu, C.-M. Hu, *Synthesis* **1996**, 997−1001.

[17] T. Ishihara, Y. Okada, M. Kuroboshi, T. Shinozaki, T. Ando, *Chem. Lett.* **1988**, 819−822.

[18] [18a] P. Doussot, C. Portella, *J. Org. Chem.* **1993**, *58*, 6675−6680. [18b] B. Dondy, C. Portella, *J. Org. Chem.* **1993**, *58*, 6671−6674. [18c] B. Dondy, P. Doussot, C. Portella, *Synthesis* **1992**, 995−998. [18d] B. Dondy, C. Portella, *Tetrahedron Lett.* **1991**, *32*, 83−86.

[19] B. Dondy, P. Doussot, M. Iznaden, M. Muzard, C. Portella, *Tetrahedron Lett.* **1994**, *35*, 4357−4360.

[20] [20a] J.-P. Bouillon, B. Didier, B. Dondy, P. Doussot, R. Plantier-Royon, C. Portella, *Eur. J. Org. Chem.* **2001**, 187−192. [20b] B. Dondy, P. Doussot, C. Portella, *Tetrahedron Lett.* **1994**, *35*, 409−412.

[21] R. Plantier-Royon, C. Portella, *Tetrahedron Lett.* **1996**, *37*, 6113−6114.

[22] M. Koos, H. S. Mosker, *Carbohydr. Res.* **1986**, *146*, 335−341.

[23] The α-hydroperfluoro ketone is itself a synthetic equivalent of the corresponding enone. Under the conditions used in the synthesis of the heterocycles, it easily loses hydrogen fluoride and is finally converted into the heterocycle. Hence, the heterocycle synthesis could have been directly performed on the ketone/

enone mixture, as we have observed in further applications (see ref.[28])
[24] A. R. Katritzky, D. L. Ostercamp, T. I. Yousaf, *Tetrahedron* **1987**, *43*, 5171−5186.
[25] [25a] G. Alvernhe, D. Greif, B. Langlois, A. Laurent, I. Le Dréan, M. Pulst, A. Selmi, M. Weissenfels, *Bull. Soc. Chim. Fr.* **1994**, *131*, 167−172. [25b] A. Laurent, I. Le Dréan, A. Selmi, *Tetrahedron Lett.* **1991**, *32*, 3071−3074.
[26] G. Alvernhe, A. Laurent, I. Le Dréan, A. Selmi, *Tetrahedron Lett.* **1993**, *34*, 2483−2486.
[27] G. Alvernhe, B. Langlois, A. Laurent, I. Le Dréan, A. Selmi, M. Weissenfels, *Tetrahedron Lett.* **1991**, *32*, 643−646.
[28] F. Chanteau, R. Plantier-Royon, C. Portella, *Synlett* **2004**, 512−516.

Received October 17, 2003

