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A Convenient Method for the Synthesis of Stable α-Fluoro Enamines of Nucleobases

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Treatment of a whole set of nucleic acid bases and related derivatives **4**, **9** and **10** with electron-deficient hexafluoropropene or 1,1,3,3,3-pentafluoropropene in the presence of sodium hydride gave the corresponding N^1 and N^9 stable fluorinated enamines with high regioselectivity. This alkylation is a result of a Michael type addition–elimination process and gave the desired products **2a**–**10a** and **2b**–**10b** as *E*/*Z* mixtures. Unexpectedly, treatment of **2b** with *tert*-butyllithium and subsequently with [D_4]methanol gave different results for *E* and *Z* stereoisomers.

Introduction

Fluoroorganic compounds have a wide scope of applications, being important pharmaceuticals, plant protection agents, modified compounds and components of a variety of polymers.[1] Selective introduction of fluorine or fluorine-containing groups into biologically active molecules can substantially change their physical, chemical and biological properties, converting them into effective agents in many areas of biology and biochemistry.[2]

As we have shown recently, the lithiated derivatives of both electron-rich and electron-poor pyrimidines react at low temperatures with the nucleophilically susceptible hexafluoropropene (HFP) to give the appropriate 5- and 6-substituted pentafluoropropenyl derivatives in addition–elimination reactions. We have also performed the reaction of a tribenzoyl derivative of inosine, with an unblocked N^1 position, with HFP in the presence of LDA. The only product of the reaction was the N^1-perfluoroenamine of this nucleoside, rather than the perfluorinated olefin (Figure 1).[3]

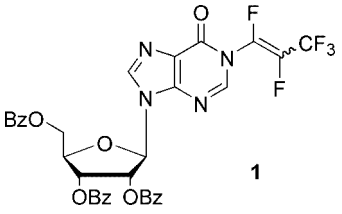

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Figure 1. N^1-(Perfluoroprop-1-enyl) derivative of tribenzoylinosine.

Fluorine-containing enamines are versatile building blocks for the introduction of fluorinated groups into various heterocyclic compounds and natural products.[4] There are many literature reports of classical methods of synthesis of α-fluoroenamines and trifluoromethyl-enamines based on the reactions of fluoro- and perfluoroalkenes[5] or 1*H*-perfluoroalkynes[6] with secondary amines, but α-fluoroenamines readily react with water to give the corresponding amides and hydrogen fluoride in an addition–elimination process.[7] Compound **1**, however, was absolutely stable and did not undergo hydrolysis on contact with water.

Enamines of nucleic acid bases have generally been obtained only in low-yielding, multi-step procedures, and only recently have effective and simple methods for the synthesis of *N*-vinyl derivatives of all nucleic acid bases been developed.[8] In the chemistry of nucleic acid derivatives, N^1-vinylpyrimidines and N^9-vinylpurines are important starting materials for syntheses of polymeric analogues of nucleic acids[9] and also in the synthesis of nucleoside analogues through 1,3-dipolar cycloaddition reactions with relevant nitrones,[10] nitrile oxides[11] and pyrrolidine 1-oxide.[12] Recently a new class of nucleoside analogues has been obtained through 1,3-dipolar cycloaddition reactions between N^1-allene derivative of thymine and nitrones.[13] These compounds show promising biological activities in vivo and are potential antiviral drugs.

This paper reports a simple one-pot procedure for obtaining *N*-α,β-difluoro-β-trifluoromethyl enamines and *N*-α-fluoro-β-trifluoromethyl enamines of uracil (**2**), thymine (**3**), 5-fluorouracil (**4**), cytosine (**5**), adenine (**6**) and guanine (**7**). The compounds were obtained with high regioselectivity for N^9 in the purine case and N^1 in that of pyrimidines. The above enamines were obtained by treatment of the nucleobases with sodium hydride, followed by hexafluoropropene (HFP) and 1,1,3,3,3-pentafluoropropene (PFP). To the best of our knowledge, the literature gives only a few examples of syntheses of enamines of nucleobases with fluorine or fluorinated substituents in the enamine moiety. On treatment of thymine and uracil with 2-bromo-3,3,3-trifluo-

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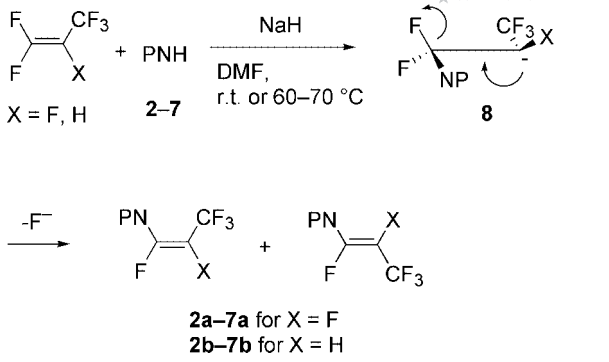
ropropene, Jiang obtained the corresponding β-trifluoromethyl enamines as mixtures of *E* and *Z* stereoisomers,[14] while Zemlicka obtained the *Z* and *E* isomers of *N*-[3-(or 2)-fluoro-2-(hydroxymethyl)cyclopropylidene]methylpurines and -pyrimidines and assessed their antiviral activities.[15] On treatment of 2′-deoxy-5-iodouridine with 3,3,3-trifluoropropyne in the presence of a palladium catalyst, Sigurdsson obtained 2′-deoxy-N^3-(3,3,3-trifluoropropenyl)-uridine instead of the expected coupling product.[16] We have not found any literature report involving the production of a purine or pyrimidine α-fluoroenamine or a stable (not undergoing hydrolysis) α-fluoroenamine. The only reported α-haloenamines of nucleic acid bases were the mono-, di- and trichloroenamines of purine and pyrimidine bases obtained by Zemlicka.[17]



Scheme 1. Addition–elimination reactions of PNH with HFP and PFP, where PNH is the appropriate pyrimidine **2**–**5** or purine **6** or **7** with endocyclic N^1 for pyrimidines and endocyclic N^9 for purines.

Results and Discussion

HFP and PFP are both highly susceptible to nucleophilic attack, as the strongly electron-withdrawing CF_3 group is responsible for a large electron deficit in the double bond. Treatment of these olefins with the sodium salts of purines and pyrimidines **2**–**7** give the corresponding fluorinated enamines of these bases, generally in good yields (Figure 2).

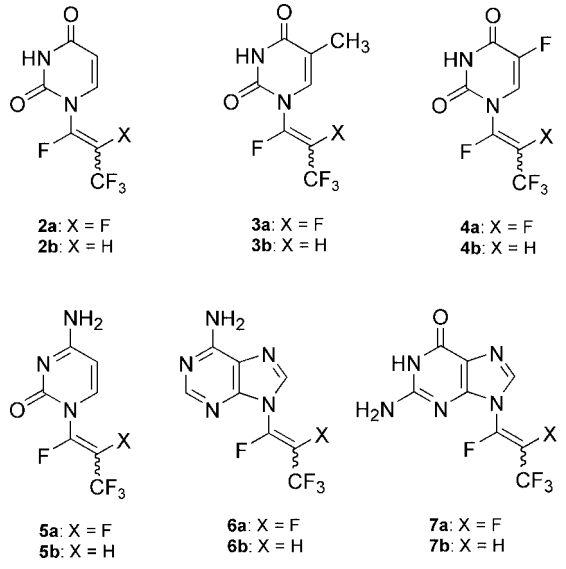


Figure 2. Fluorinated enamines of nucleobases.

Nucleophilic substitution is regioselective towards olefin and takes place exclusively at CF_2= (the most positive site) and not at =$CFCF_3$ or =$CHCF_3$. In the carbanion transition state **8** (Scheme 1) the negative charge is localised on the carbon atom, strongly stabilised by the CF_3 group, and the elimination of the fluoride ion leads to the unsaturated system and consequently in this addition–elimination sequence to the enamine.

The purine and pyrimidine bases were converted into the corresponding sodium salts with NaH in DMF (at room temperature or at 70 °C), after which the appropriate fluorinated olefin was slowly passed through the solution. Standard workup of the reaction mixture gave the products **2a**–**7a** and **2b**–**7b**, respectively, as mixtures of *E* and *Z* stereoisomers (Table 1). The addition–elimination reaction was not significantly stereoselective, although in the majority of compounds the more thermodynamically stable isomer was prevalent (high *E*/*Z* ratios in the series of enamines obtained in the reactions with HFP and high *Z*/*E* ratios in the series obtained in the reactions with PFP). Only for compound **4a** was a small prevalence of the less thermodynamically stable *Z* isomer observed.

Table 1. Preparation of enamines **2a**–**10a** and **2b**–**10b** by addition–elimination reactions of HFP and PFP with nucleobases.

Entry	Compound	Conditions	Yield	Isomer ratio
1	**2a**	room temp.	38	*E*/*Z* 52:48
		70 °C	71	*E*/*Z* 52:48
2	**3a**	room temp.	41	*E*/*Z* 58:42
		70 °C	75	*E*/*Z* 55:45
3	**4a**	room temp.	43	*E*/*Z* 48:52
		70 °C	80	*E*/*Z* 45:55
4	**5a**	room temp.	12	*E*/*Z* 50:50
		70 °C	44	*E*/*Z* 50:50
5	**6a**	room temp.	31	*E*/*Z* 66:34
		70 °C	53	*E*/*Z* 66:34
6	**7a**	room temp.	66	*E*/*Z* 52;48
		70 °C	71	*E*/*Z* 55:45
7	**2b**	70 °C	82	*Z*/*E* 62:38
8	**3b**	70 °C	75	*Z*/*E* 60:40
9	**4b**	70 °C	86	*Z*/*E* 62:38
10	**5b**	70 °C	67	*Z*/*E* 65:35
11	**6b**	70 °C	52	*Z*/*E* 60:40
12	**7b**	70 °C	59	*Z*/*E* 68:32
13	**9a**	room temp.	44	*E*/*Z* 54:46
		70 °C	68	*E*/*Z* 50:50
14	**10a**	room temp.	– (76[b])	*E*/*Z* 64:36
		70 °C	12[a] (91[b])	*E*/*Z* 70:30
15	**9b**	70 °C	89	*Z*/*E* 77:23
16	**10b**	70 °C	78[a]	*Z*/*E* 58:42

[a] Unstable product. [b] ^{19}F NMR yields.

The formation of two *E* and *Z* stereoisomers and the greater *E* selectivity of the enamines obtained on treatment with HFP, together with the *Z* selectivity of the enamines obtained on treatment with PFP, can be explained by analysis of the conformation of carbanion **8**. Elimination of fluoride anion from the two possible transition states A and B of carbanion **8** gives the *E* and the *Z* stereoisomers. In the transition state A, leading to the more stable stereoisomer, two large groups – that is, a heterocyclic ring and CF_3 – are in the convenient *anti* arrangement and are free from steric interactions, while in the transition state B leading to the less stable stereoisomer these groups are in a *syn* arrangement (Figure 3).

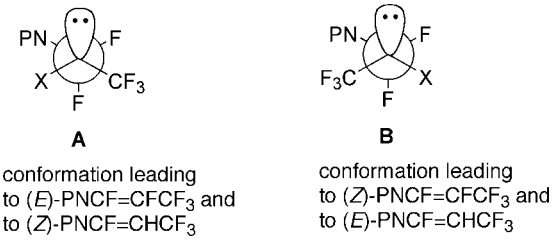


Figure 3. Two possible transition states of carbanion **8**.

The *E*/*Z* stereochemistries of the obtained enamines were established by ^{19}F NMR analysis; the results are given in Table 1. For the pentafluoropropenyl derivatives of the RCF=CFCF$_3$ type the *trans* coupling constant is much higher than the *cis* one. In general, typical literature $^3J_{F,F}$(*trans*) coupling constants range from 130 to 144 Hz, while $^3J_{F,F}$(*cis*) ones go only from 9 to 13 Hz,[18] so the assignment of the coupling constants and chemical shifts to all fluorine atoms in a mixture of two *E* and *Z* pentafluoropropenyl isomers can easily be established. The ^{19}F NMR spectra of *N*-α,β-difluoro-β-trifluoromethyl enamines PNCF=CFCF$_3$ show the coupling constants $^3J_{F,F}$(*trans*) = 131–133 Hz and $^3J_{F,F}$(*cis*) = 12 Hz. Similarly, for the *N*-α-fluoro-β-trifluoromethyl enamines PNCF=CHCF$_3$, the $^3J_{H,F}$(*trans*) coupling constants range from 27 to 32 Hz, whereas $^3J_{H,F}$(*cis*) = 4–6 Hz.

For the series of *N*-α,β-difluoro-β-trifluoromethylenamines (compounds **2a**–**7a**, **9a** and **10a**) the reactions were carried out both at room temperature and at 70 °C. The temperature variation significantly influenced the reaction yield but had practically no influence on the ratios of the isomers, so the reactions are not kinetically controlled. Because of the dramatically low solubility of guanine in DMF, it was first converted into the soluble trimethylsilyl derivative and then into its sodium salt, which reacted with HFP to give the desired enamine **7a**. Attempts were made to obtain the cytosine and adenine enamines from their derivatives blocked on the exocyclic nitrogen atoms in order to enhance their solubilities. Treatment of N^4-benzoylcytosine (**9**) and N^6-benzoyladenine (**10**) with HFP indeed led to the desired fluorinated enamines **9a** and **10a** (Figure 4) in good yields (Entries 13 and 14), but attempts at their deprotection failed.

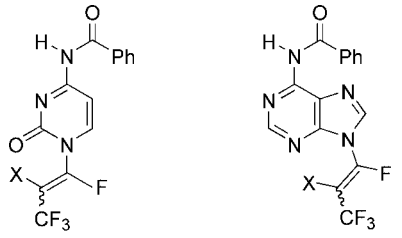
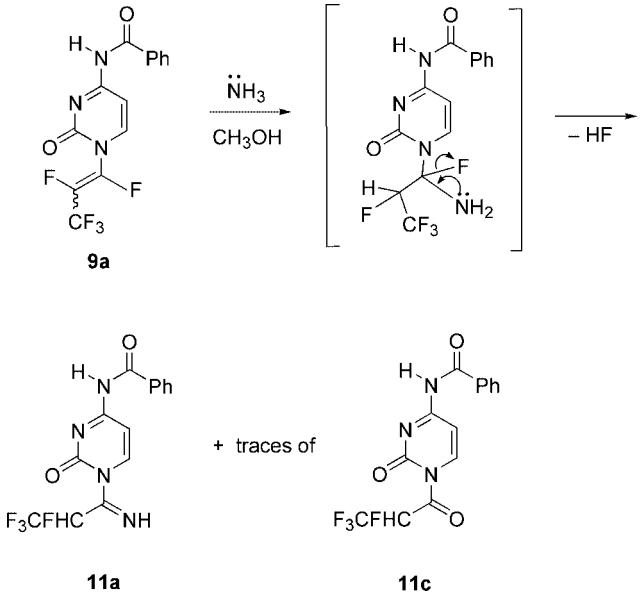


Figure 4. Fluorinated enamines of adenine and cytosine blocked on the exocyclic nitrogen atoms.

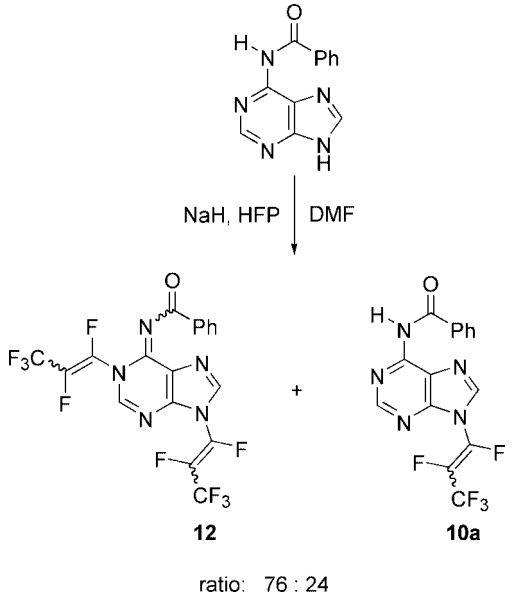
The standard deprotection procedure with the benzoyl derivative **9a** (to give **5a**) in methanolic ammonia gave, instead of the desired product, compound **11a** (Scheme 2) as a result of an addition–elimination process (*m*/*z* = 342 [M]$^+$, two signals in ^{19}F NMR; a doublet of doublets at –74.06 ppm, 3 F, J_1 = 12, J_2 = 7 Hz and a doublet of quartets at –203.56 ppm, 1 F, J_1 = 12, J_3 = 44Hz), contaminated with a small amount of by-product, most probably **11c** (two signals in ^{19}F NMR; a doublet of doublets at –74.33 ppm, 3 F, J_1 = 12, J_2 = 7 Hz and a multiplet at –203.94 ppm, 1 F).



Scheme 2.

The above reaction reveals a high susceptibility of the enamine double bond, strongly activated with the electron-withdrawing CF_3 group, to the attack of a not particularly strong nucleophile such as NH_3. Moreover, compound **10a** is unstable and when left with access to the air, it relatively rapidly undergoes hydrolysis to an amide insoluble in water, methanol and chloroform, the ^{19}F NMR spectrum of which shows a characteristic pattern of the structure PNC(O)-CHFCF$_3$ (a doublet of doublets at –74.03 ppm, 3 F, J_1 = 11, J_2 = 7 Hz and a doublet of quartets at –202.87 ppm, 1 F, J_1 = 11, J_3 = 45 Hz). The process of decomposition of

10a, as monitored by ^{19}F NMR spectroscopy, involved at first the degradation of the *Z* isomer (leading to the disappearance of its signal in the ^{19}F NMR spectrum) and the slightly slower diminishing of the *E* isomer. N^6-Benzoyladenine is also the most susceptible to dialkylation in the presence of a molar excess of sodium hydride; the main product of the reaction between this compound and HFP is the dialkenyl derivative (*m*/*z* = 499 $[M]^+$, a complex ^{19}F NMR spectrum). The alkylation of N^6-benzoyladenosine derivatives with allyl bromide gives mixtures of N^1- and N^6-alkylation products.[19] In the ^1H NMR spectra of N^1- and N^6-alkylated products, significant differences in the chemical shifts of the C^2–H and C^8–H protons are reported. Analysis of the ^{19}F NMR spectrum of our isolated compound **12** showed that not a mixture, but only one dialkylation product, had been obtained. The ^{19}F NMR spectrum of this product revealed almost identical chemical shifts of the two (*E*)-F^α atoms and very similar chemical shifts of the two (*E*)-F^β atoms, which, we believe, excludes alkylation of the exocyclic nitrogen atom. In view of the chemical shifts of C^2–H and C^8–H in the ^1H NMR spectrum and the chemical shifts of F^α and F^β in the ^{19}F NMR spectrum, compound **12** is suggested to be a N^1,N^9-dialkylation product (Scheme 3). The other purine and pyrimidine bases gave dialkenyl derivatives only in small amounts or not at all, irrespective of the excess of the hydride used.



Scheme 3. The reaction between compound **10** and HFP in the presence of a fourfold excess of NaH.

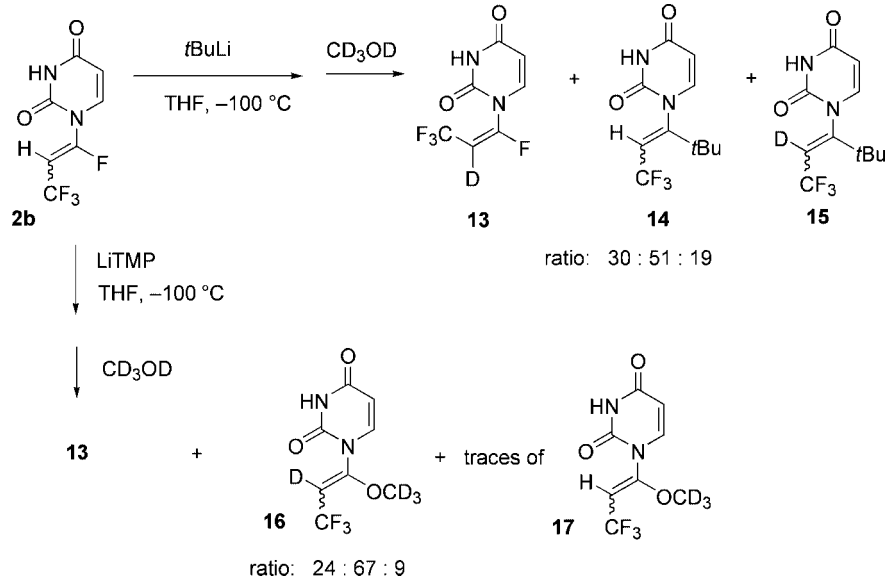
The reactions performed at a room temperature also gave some quantities of addition products as side products. Increasing the reaction temperature to 70 °C practically eliminated this problem, and the percentage contents of addition products decreased to less than 3%, or below the limits of detection by ^{19}F NMR spectroscopy. We did not observe any traces of allyl substitution; the intermediate carbanions **8** exclusively eliminated fluoride from the $PNCF_2$ group and not from the CF_3 group.

For the series of *N*-α-fluoro-β-trifluoromethylenamines (compounds **2b**–**7b**, **9b** and **10b**) no products formed as a result of dialkylation of purine and pyrimidine bases were detected. The reactions with PFP were much cleaner than those with HFP, which is a consequence of the nucleophilicity of PFP being lower than that of HFP and total selectivity of the substitution reaction towards the more basic nitrogen. Moreover, the mixtures of stereoisomers of compounds **2a**–**7a**, **9a** and **10a** were chromatographically not differentiated and gave single spots on TLC, irrespective of the developing system, whereas the mixtures of stereoisomers of compounds **2b**–**7b** gave separate TLC spots. The separation was visible, although the differences in the polarities of the *E* and *Z* stereoisomers was too low to permit their separation on a chromatographic column. However, column separation was successfully accomplished for derivatives **9b** and **10b**. Unfortunately, compound **10b** – in particular (*Z*)-**10b** – was unstable, just like **10a**, and underwent slow decomposition after isolation.

The only reasonable explanation for the notable differences in polarity and chromatographic separability of *E* and *Z* stereoisomers would seem to be the presence of weak interactions between the C^β–H proton of the tetrafluoropropenyl group and the lone-pair electrons on the oxygen atom C^2=O in pyrimidines and on the nitrogen N^3 in purines. Such an interaction is often called the non-conventional hydrogen bond.[20]

We expected that *N*-α-fluoro-β-trifluoromethylenamines, just like PFP, should undergo lithiation at low temperatures to give the corresponding products with electrophiles. On treatment of PFP with LDA or *t*BuLi and subsequently with $ZnCl_2$, CdI_2 and CF_3CO_2Ag, Burton obtained practically quantitatively the corresponding zinc, silver and cadmium reagents, which were next functionalised in alkylation, arylation, halogenation and oxidative coupling reactions.[21] Our attempts at lithiation of compound **2b** and further conversion of the lithiated enamine into the desired derivatives failed. It was difficult to characterise the reaction mixtures or the mixtures with total decomposition of the fluorinated substrate. However, we assume that the simple lithiation reactions of compound **2b** performed at –100 °C in THF and subsequently quenched with deuterated methanol (CD_3OD) point to the reason for the differences in the reactivities of **2b** and PFP. Scheme 4 presents the courses of these reactions and the obtained products **13**–**17**.

Interestingly, treatment of compound **2b** with excess *t*BuLi gave different results for the *E* and the *Z* stereoisomers. The *E* stereoisomer, with the C^β–H proton not involved in a hydrogen bond, reacted as expected, so as a result of proton abstraction it gave a lithiated derivative that was quenched by CD_3OD to give compound **13**, with the preserved double bond configuration. The $^4J_{F,F}$ coupling constant in ^{19}F NMR spectra of **13** was 12 Hz, which means that the fluorine atom and the CF_3 group are in a *trans* relationship with respect to one another (for the *cis* arrangement $^4J_{F,F}$ = 17–18 Hz). In the *Z* stereoisomer in which the proton is engaged in an interaction with the car-



Scheme 4. Different routes for reactions of (*E*)- and (*Z*)-(tetrafluoroprop-1-enyl)uracil **2b** with *t*BuLi and LiTMP.

bonyl group, *t*BuLi behave as a typical nucleophile,[22] giving a mixture of addition–elimination products **14** and **15** as a result of the reaction with CD_3OD. Lithium tetramethylpiperidide (LiTMP), a strong, sterically crowded and non-nucleophilic base, also gave compound **13** in its reaction with the *E* stereoisomer. The *Z* stereoisomer did not react with LiTMP, and only after addition of CD_3OD is a strong nucleophile generated in situ, giving compound **16**, together with a small amount of compound **17**.

Compound **13** and the mixtures of **14/15** and **16/17** were fully characterised by ^{19}F NMR, ^{1}H NMR and MS. As follows from MS spectral analysis, only compound **13** shows retro-Diels–Alder (RDA) fragmentation as the main fragmentation path [M – RDA (100%)]$^+$, while for compounds **14/15** and **16/17** the RDA or RDA – *t*Bu fragmentation gives peaks of very low abundances.

The C^{β}–H proton, as was expected, did not undergo isotopic exchange with D_2O in ^{1}H NMR spectroscopy experiments. However, ^{1}H NMR spectra taken in $CDCl_3$ and [D_6]DMSO provided evidence of interactions between C^{β}–H···O=C^2 and Cβ–H···N^3 in the *Z* stereoisomers of compounds **2b**–**7b**, **9b** and **10b**. In $CDCl_3$, the intramolecularly bonded C^{β}–H protons in the *Z* stereoisomers are insignificantly shifted towards lower field relative to the C^{β}–H protons in the *E* stereoisomers. In [D_6]DMSO, being a strong proton acceptor in the intermolecular hydrogen bond, the situation is the reverse, and the C^{β}–H protons in the *E* stereoisomers, not involved in any intramolecular interactions, are more strongly shifted towards lower field than those in the *Z* stereoisomers (see Exp. Section).

X-ray analysis of crystals of (*Z*)-**9b**[23] revealed that the molecules are conformationally disordered at 296 K. The tetrafluoropropenyl substituent assumes two positions in the molecule, rotated by ca. 180° about the N(1)–C(7) bond, and the terminal fluorine atoms apparently also possess the freedom to rotate about the C(8)–C(9) bond, as illustrated in Figure 5. Otherwise, the (*Z*)-**9b** molecule is nearly planar in the crystal structure: the best planes fitted to the phenyl and pyrimidinone rings are inclined by 7.2(2)°, and the two sites of the tetrafluoropropenyl substituent are also nearly coplanar with the pyrimidinone ring. The intramolecular C(8a)–H(8a)···O(2) hydrogen-bond-like contact (C–H 0.94 Å, H···O 2.556 Å, C···O 2.931 Å and C–H···O 104.1°) is too weak to counteract the factors destabilizing the molecular conformation. In the crystal structure the molecules are linked into zig-zag chains along [010] by weak N(4)–H(4)···O(2^{i}) hydrogen bonds (N–H 0.91 Å, H···O 2.130 Å, N···O 3.019 Å and N–H···O 164.6°; symmetry code (i): 0.5 – *x*, 0.5 + *y*, 0.5 – *z*).

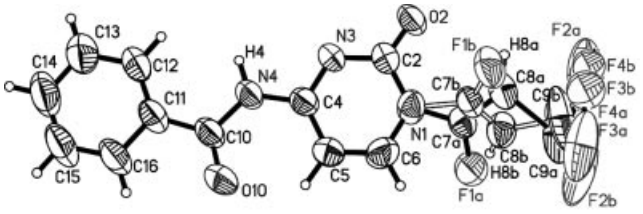


Figure 5. The molecule of (*Z*)-**9b** viewed in perpendicular to its average plane. Two positions of the tetrafluoropropenyl substituent have been indicated, one with the full and the other with open bonds. The thermal ellipsoids are indicated at the 50% probability level.

Conclusions

In summary, we have successfully developed a simple method for the preparation of stable *N*-α,β-difluoro-β-trifluoromethyl enamines and *N*-α-fluoro-β-trifluoromethyl enamines of nucleic acids bases from the readily available HFP and PFP. The reactions could be performed under very mild conditions and with simple manipulations, giving

the desired products in moderate or high yields. In view of the role of vinylpyrimidines and vinylpurines in the synthesis of cyclic and acyclic analogues of nucleosides, the reactions described above afforded two series of differently fluorinated versatile intermediates that might represent useful starting materials for biologically interesting molecules. Different functionalisation reactions of compounds **2a**–**7a** and **2b**–**7b** will be a subject of future work.

Experimental Section

General Remarks: N^4-Benzoylcytosine (**9**) and N^6-benzoyladenine (**10**) were prepared as described in Refs.[24,25] All other starting materials and reagents were obtained from Fluka or Sigma–Aldrich. Hexafluoropropene and 1,1,3,3,3-pentafluoropropene were purchased from SynQuest Labs Inc. Dimethylformamide was distilled from P_2O_5 and was stored over molecular sieves (0.4 nm). Thin layer chromatography was performed with 60 F_{254} TLC plates (Merck). Column chromatography was performed with silica gel (Merck, particle size 0.063–0.200 mm, 70–230 mesh). All reactions were carried out under argon. The reaction temperature of –100 °C was achieved by cooling with a N_2/hexane bath

^{1}H and ^{19}F NMR spectra were recorded with a Varian Gemini 300 MHz spectrometer (300.069 MHz for ^{1}H and 282.318 MHz for ^{19}F) in $CDCl_3$, $CDCl_3$ + CD_3OD and [D_6]DMSO as solvents. TMS was the internal standard for ^{1}H NMR spectroscopy, while $CFCl_3$ was used as a reference for ^{19}F NMR spectroscopy. Chemical shifts for ^{1}H NMR are reported in ppm downfield from TMS and those for ^{19}F NMR upfield from $CFCl_3$. The mass spectra were recorded on a AMD 402 spectrometer, ionisation was achieved through electron impact (EI). The elemental analyses were performed on a Perkin–Elmer apparatus. Melting points were determined on a Boetius apparatus and are reported uncorrected.

General Procedure for 2a–10a and 2b–10b: A nucleobase (**2**–**10**, 2 mmol) was dissolved or suspended in DMF (5–15 mL) at 60 °C. The solution was cooled to room temperature, and NaH (60% oil suspension; 2.5–4 mmol) was added under argon. The mixture was stirred until evolution of H_2 had ceased. The reaction mixture was once more heated to 70 °C, and hexafluoropropene or 1,1,3,3,3-pentafluoropropene (approximately 6 mmol) was added through a Carrius tube. The mixture was kept at 70 °C for 15–30 minutes. After cooling to room temperature the crude reaction mixture was poured into water (30 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined extracts were washed with brine and dried with Na_2SO_4. Only in the cases of compounds **5a** and **5b** was the crude reaction mixture directly extracted into CH_2Cl_2 after neutralization with methanolic HCl. After removal of solvents under reduced pressure the residue was purified by silica gel column chromatography (silica gel, a gradient of hexane/CH_2Cl_2, CH_2Cl_2, a gradient of CH_2Cl_2/MeOH) to give a mixture of *E*/*Z* enamines.

***N*^{1}-(Perfluoroprop-1-enyl)uracil (2a):** Compound **2** (224 mg, 2 mmol) gave **2a** (343 mg, 71% yield) as a colourless solid. M.p. 135–140 °C. ^{1}H NMR (300 MHz, [D_6]DMSO, 25 °C): δ = 5.95 (m, 1 H, C^5–H), 7.96 (m, 1 H, C^6–H), 12.06 (br. s, 1 H, N^3–H) ppm. ^{19}F NMR (282 MHz, [D_6]DMSO, 25 °C): for *E* isomer: δ = –67.51 (dd, *J* = 11 and 22 Hz, 3 F, CF_3), –114.41 (dq, *J* = 22 and 132 Hz, 1 F, F^α), –164.98 (dd, *J* = 11 and 132 Hz, 1 F, F^β) ppm; for *Z* isomer: δ = –68.08 (dd, *J* = 10 and 12 Hz, 3 F, CF_3), –94.45 (m, 1 F, F^α), –154.65 (m, 1 F, F^β) ppm. MS (EI): *m*/*z* = 242 $[M]^+$ (12%), 199 (100%). $C_7H_3F_5N_2O_2$ (242.12): calcd. C 34.73, H 1.25, N 11.57; found C 34.55, H 1.33, N 11.36.

N^1-(Perfluoroprop-1-enyl)thymine (3a): Compound **3** (252 mg, 2 mmol) gave **3a** (384 mg, 75% yield) as a colourless solid. M.p. 102–105 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.99 (m, 3 H, CH_3), 7.01 (m, 1 H, C^6–H), 8.91 (br. s, 1 H, N^3–H) ppm. ^{19}F NMR (282 MHz, $CDCl_3$, 25 °C): for *E* isomer: δ = –67.87 (dd, *J* = 11 and 21 Hz, 3 F, CF_3), –116.65 (dq, *J* = 21 and 132 Hz, 1 F, F^α), –161.67 (dq, *J* = 12 and 132 Hz, 1 F, F^β) ppm; for *Z* isomer: δ = –68.23 (dd, *J* = 9 and 12 Hz, 3 F, CF_3), –97.10 (m, 1 F, F^α), –150.19 (m, 1 F, F^β) ppm. MS (EI): *m*/*z* = 256 $[M]^+$ (27%), 213 (100%). $C_8H_5F_5N_2O_2$ (256.14): calcd. C 37.51, H 1.97, N 10.94; found C 37.66, H 1.81, N 11.08.

***N*^{1}-(Perfluoroprop-1-enyl)-5-fluorouracil (4a):** Compound **4** (260 mg, 2 mmol) gave **4a** (416 mg, 80% yield) as a colourless solid. M.p. 89–94 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): for *Z* isomer: δ = 7.43 (d, *J* = 6 Hz, 1 H, C^6–H), 10.04 (br. s, 1 H, N^3–H) ppm; for *E* isomer: δ = 7.39 (d, *J* = 6 Hz, 1 H, C^6–H), 10.04 (br. s, 1 H, N^3–H) ppm. ^{19}F NMR (282 MHz, $CDCl_3$, 25 °C) for *E* isomer: δ = –68.48 (dd, *J* = 11 and 22 Hz, 3 F, CF_3), –117 (dq, *J* = 22 and 132 Hz, 1 F, F^α), –161.14 (br. s, 1 F, C^5-F), –161.32 (dq, *J* = 11 and 132 Hz, 1 F, F^β) ppm; for *Z* isomer: δ = –68.83 (dd, *J* = 10 and 12 Hz, 3 F, CF_3), –98.28 (m, 1 F, F^α), –149.90 (m, 1 F, F^β), –161.14 (br. s, 1 F, C^5-F) ppm. MS (EI): *m*/*z* = 260 $[M]^+$ (26%), 217 (100%). $C_7H_2F_6N_2O_2$ (260.11): calcd. C 32.32, H 0.78, N 10.77; found C 31.93, H 1.00, N 10.62.

***N*^{1}-(Perfluoroprop-1-enyl)cytosine (5a):** Compound **5** (222 mg, 2 mmol) gave **5a** (212 mg, 44% yield) as a colourless solid. M.p. 212–220 °C. ^{1}H NMR (300 MHz, [D_6]DMSO, 25 °C): δ = 5.93 (d, *J* = 7 Hz, 1 H, C^5–H), 7.83 (d, *J* = 7 Hz, 1 H, C^6–H), 7.98 (br. s, 2 H, NH_2) ppm. ^{19}F NMR (282 MHz, $CDCl_3$ + CD_3CD, 25 °C): for *E* isomer: δ = –68.25 (m, 3 F, CF_3), –114.87 (dq, *J* = 21 and 132 Hz, 1 F, F^α), –165.49 (dq, *J* = 11 and 132 Hz, 1 F, F^β) ppm; for *Z* isomer: δ = –68.25 (m, 3 F, CF_3), –95.56 (m, 1 F, F^α), –154.36 (m,1 F, F^β) ppm. MS (EI): *m*/*z* = 241 $[M]^+$ (100%). $C_7H_4F_5N_3O$ (241.13): calcd. C 34.87, H 1.67, N 17.43; found C 34.81, H 1.54, N 17.18.

***N*^{9}-(Perfluoroprop-1-enyl)adenine (6a):** Compound **6** (270 mg, 2 mmol) gave **6a** (281 mg, 53% yield) as a colourless solid. M.p. 163–170 °C. ^{1}H NMR (300 MHz, [D_6]DMSO, 25 °C): δ = 7.75 (br. s, 2 H, NH_2), 8.27 (s, 1 H, C^2–H), 8.58 (s, 1 H, C^8–H) ppm. ^{19}F NMR (282 MHz, $CDCl_3$ + CD_3OD, 25 °C): for *E* isomer: δ = –67.95 (dd, *J* = 11 and 21 Hz, 3 F, CF_3), –117.75 (dq, *J* = 21 and 132 Hz, 1 F, F^α), –165.45 (dq, *J* = 11 and 132 Hz, 1 F, F^β) ppm; for *Z* isomer: δ = –67.98 (dd, *J* = 8 and 11 Hz, 3 F, CF_3), –94.11 (m, 1 F, F^α), –149.13 (m, 1 F, F^β) ppm. MS (EI): *m*/*z* = 265 $[M]^+$ (80%), 238 (100%). $C_8H_4F_5N_5$ (265.16): calcd. C 36.24, H 1.52, N 26.41; found C 36.36, H 1.49, N 26.07.

***N*^{9}-(Perfluoroprop-1-enyl)guanine (7a):** Compound **7** (302 mg, 2 mmol) gave **7a** (399 mg, 71% yield) as a yellowish solid. M.p. decomposition above 185 °C. ^{1}H NMR (300 MHz, [D_6]DMSO, 25 °C): δ = 6.90 (br. s, 2 H, NH_2), 8.10 (s, 1 H, C^8–H), 11.01 (br. s, 1 H, N^1–H) ppm. ^{19}F NMR (282 MHz, [D_6]DMSO, 25 °C): for *E* isomer: δ = –67.51 (dd, *J* = 11 and 21 Hz, 3 F, CF_3), –113.93 (dq, *J* = 21 and 132 Hz, 1 F, F^α), –167.44 (dq, *J* = 11 and 132 Hz, 1 F, F^β) ppm; for *Z* isomer: δ = –68.09 (dd, *J* = 8 and 11 Hz, 3 F, CF_3), –91.26 (m,1 F, F^α), –154.34 (m, 1 F, F^β) ppm. MS (EI): *m*/*z* = 281 $[M]^+$ (100%). $C_8H_4F_5N_5O$ (281.16): calcd. C 34.18, H 1.43, N 24.91; found C 33.86, H 1.31, N 24.74.

***N*^{1}-(1,3,3,3-Tetrafluoroprop-1-enyl)uracil (2b):** Compound **2** (224 mg, 2 mmol) gave **2b** (367 mg, 82% yield) as a colourless solid. M.p. 124–127 °C. ^{1}H NMR (300 MHz, [D_6]DMSO, 25 °C): for *Z* isomer: δ = 5.81 (d, *J* = 8 Hz, 1 H, C^5–H), 6.40 (dq, *J* = 7 and 27 Hz, 1 H, H^β), 7.84 (d, *J* = 8 Hz, 1 H, C^6–H), 11.88 (br. s, 1 H,

N^3–H) ppm; for *E* isomer: δ = 5.86 (d, *J* = 8 Hz, 1 H,C^5–H), 6.82 (dq, *J* = 5 and 7 Hz, 1 H, H^β), 7.90 (d, *J* = 8 Hz, 1 H, C^6–H), 11.88, (br. s, 1 H, N^3–H) ppm. ^{1}H NMR ($CDCl_3$, 25 °C): for *Z* isomer: δ = 5.90 (dq, *J* = 7 and 29 Hz, 1 H, H^β), 5.94 (d, *J* = 8 Hz, 1 H, C^5–H), 7.41 (d, *J* = 8 Hz, 1 H, C^6–H), 9.07 (br. s, 1 H, N^3–H); for *E* isomer: δ = 5.87 (m, 1 H, H^β), 5.91 (d, *J* = 8 Hz, 1 H,C^5–H), 7.19 (d, *J* = 8 Hz, 1 H, C^6–H), 9.07, (br. s, 1 H, N^3–H) ppm. ^{19}F NMR (282 MHz, [D_6]DMSO, 25 °C) for *Z* isomer: δ = –56.75 (dd, *J* = 8 and 18 Hz, 3 F, CF_3), –76.51 (dq, *J* = 18 and 27 Hz, 1 F, F^α) ppm; for *E* isomer: –57.98 (dd, *J* = 7 and 13 Hz, 3 F, CF_3), –72.82 (dq, *J* = 5 and 13 Hz, 1 F, F^α) ppm. ^{19}F NMR ($CDCl_3$, 25 °C): for *Z* isomer: δ = –58.11 (dd, *J* = 8 and 18 Hz, 3 F, CF_3), –86.30 (dq, *J* = 18 and 29 Hz, 1 F, F^α); for *E* isomer: –59.61 (dd, *J* = 7 and 13 Hz, 3 F, CF_3), –74.38 (dq, *J* = 5 and 13 Hz, 1 F, F^α) ppm. MS (EI): *m*/*z* = 224 $[M]^+$ (18%), 181 (100%). $C_7H_4F_4N_2O_2$ (224.12): calcd. C 37.51, H 1.80, N 12.45; found C 37.21, H 1.98, N 12.09.

N^1-(1,3,3,3-Tetrafluoroprop-1-enyl)thymine (3b): Compound **3** (252 mg, 2 mmol) gave **3b** (357 mg, 75% yield) as a colourless solid. M.p. 105–108 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): for *Z* isomer: δ = 2.90 (s, 3 H, CH_3), 5.89 (dq, *J* = 7 and 27 Hz, 1 H, H^β), 7.25 (s, 1 H, C^6–H), 9.80 (br. s, 1 H, N^3–H) ppm; for *E* isomer: δ = 2.90 (s, 3 H, CH_3), 5.83 (m, 1 H, H^β), 7.00 (s, 1 H, C^6–H), 9.80 (br. s, 1 H, N^3–H) ppm. ^{19}F NMR (282 MHz, $CDCl_3$, 25 °C): for *Z* isomer: δ = –58.04 (dd, *J* = 7 and 18 Hz, 3 F, CF_3), –86.76 (dq, *J* = 17 and 29 Hz, 1 F, F^α) ppm; for *E* isomer: –59.77 (dd, *J* = 5 and 12 Hz, 3 F, CF_3), –74.56 (dq, *J* = 4 and 12 Hz, 1 F, F^α) ppm. MS (EI): *m*/*z* = 238 $[M]^+$ (40%), 195 (100%). $C_8H_6F_4N_2O_2$ (238.15): calcd. C 40.35, H 2.54, N 11.76; found C 40.50, H 2.24, N 11.96.

N^1-(1,3,3,3-Tetrafluoroprop-1-enyl)-5-fluorouracil (4b): Compound **4** (260 mg, 2 mmol) gave **4b** (368 mg, 76% yield) as a colourless solid. M.p. 144–151 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): for *Z* isomer: δ = 5.79 (dq, *J* = 7 and 30 Hz, 1 H, H^β), 7.54 (d, *J* = 6 Hz, 1 H, C^6–H), 10.34 (br. s, 1 H, N^3–H) ppm; for *E* isomer: 5.88 (m, 1 H, H^β), 7.29 (d, *J* = 6 Hz, 1 H, C^6–H), 10.34 (br. s, 1 H, N^3–H) ppm. ^{19}F NMR (282 MHz, $CDCl_3$, 25 °C): for *Z* isomer: δ = –58.05 (dd, *J* = 7 and 18 Hz, 3 F, CF_3), –88.05 (dq, *J* = 18 and 30 Hz, 1 F, F^α), –161.30 (d, *J* = 6 Hz, 1 F, C^5-F) ppm; for *E* isomer: δ = –59.88 (dd, *J* = 7 and 13 Hz, 3 F, CF_3), –75.47 (dq, *J* = 4 and 13 Hz, 1 F, F^α), –162.52 (d, *J* = 6 Hz, 1 F, C^5-F) ppm. MS (EI): *m*/*z* = 242 $[M]^+$ (44%), 199 (100%). $C_7H_3F_5N_2O_2$ (242.12): calcd. C 34.73, H 1.25, N 11.57; found C 34.40, H 1.20, N 11.19.

N^1-(1,3,3,3-Tetrafluoroprop-1-enyl)cytosine (5b): Compound **5** (222 mg, 2 mmol) gave **5b** (299 mg, 67% yield) as a yellowish solid. M.p. 168–173 °C. ^{1}H NMR (300 MHz, [D_6]DMSO, 25 °C): for *Z* isomer: δ = 5.87 (d, *J* = 7 Hz, 1 H, C^5–H), 6.31 (dq, *J* = 8 and 27 Hz, H^β), 7.72 (d, *J* = 7 Hz, 1 H, C^6–H), 7.86 (br. s, 2 H, NH_2) ppm; for *E* isomer: δ = 5.87 (d, *J* = 7 Hz, 1 H, C^5–H), 6.56 (m, 1 H, H^β), 7.71 (d, *J* = 7 Hz, 1 H, C^6–H), 7.86 (br. s, 2 H, NH_2) ppm. ^{19}F NMR (282 MHz, [D_6]DMSO, 25 °C): for *Z* isomer: δ = –56.19 (dd, *J* = 8 and 18 Hz, 3 F, CF_3), –76.26 (dq, *J* = 18 and 28 Hz, 1 F, F^α) ppm; for *E* isomer: δ = –57.23 (dd, *J* = 7 and 14 Hz, 3 F, CF_3), –70.48 (dq, *J* = 5 and 14 Hz, 1 F, F^α) ppm. MS (EI): *m*/*z* = 223 $[M]^+$ (100%). $C_7H_5F_4N_3O$ (223.14): calcd. C 37.68, H 2.26, N 18.83; found C 37.36, H 2.42, N 18.48.

N^9-(1,3,3,3-Tetrafluoroprop-1-enyl)adenine (6b): Compound **6** (270 mg, 2 mmol) gave **6b** (257 mg, 52% yield) as a colourless solid. M.p. 150–155 °C. ^{1}H NMR (300 MHz, [D_6]DMSO, 25 °C): for *Z* isomer: δ = 6.68 (dq, *J* = 7 and 32 Hz, 1 H, H^β), 7.72 (s, 2 H, NH_2), 8.32 (s, 1 H, C^2–H), 8.58 (s, 1 H, C^8–H) ppm; for *E* isomer: 7.02 (dq, *J* = 6 and 7 Hz, 1 H, H^β), 7.61 (s, 2 H, NH_2), 8.24 (s, 1 H, C^2–H), 8.51 (s, 1 H, C^8–H) ppm. ^{19}F NMR (282 MHz, [D_6]-DMSO, 25 °C): for *Z* isomer: δ = –54.38 (dd, *J* = 7 and 17 Hz, 3 F, CF_3), –90.48 (dq, *J* = 17 and 32 Hz, 1 F, F^α) ppm; for *E* isomer: δ = –57.18 (dd, *J* = 7 and 14 Hz, 3 F, CF_3), –70.86 (dq, *J* = 6 and 14 Hz, 1 F, F^α) ppm. MS (EI): *m*/*z* = 247 $[M]^+$ (100%). $C_8H_5F_4N_5$ (247.16): calcd. C 38.88, H 2.04, N 28.34; found C 38.54, H 2.42, N 28.05.

N^9-(1,3,3,3-Tetrafluoroprop-1-enyl)guanine (7b): Compound **7** (302 mg, 2 mmol) gave **7b** (310 mg, 59% yield) as a yellowish solid. M.p.; decomposition from 176 °C. ^{1}H NMR (300 MHz, [D_6]-DMSO, 25 °C): for *Z* isomer: δ = 6.60 (dq, *J* = 8 and 32 Hz, 1 H, H^β), 6.95 (br. s, 2 H, NH_2), 8.10 (s, 1 H, C^8–H), 11.04 (br. s, 1 H, N^1–H) ppm; for *E* isomer: δ = 6.80 (m, 1 H, H^β), 6.95 (br. s, 2 H, NH_2), 8.01 (s, 1 H, C^8–H), 10.94 (br. s, 1 H, N^1–H) ppm. ^{19}F NMR (282 MHz, [D_6]DMSO, 25 °C): for *Z* isomer: δ = –54.41 (dd, *J* = 8 and 18 Hz, 3 F, CF_3), –89.11 (dq, *J* = 17 and 32 Hz, 1 F, F^α) ppm; for *E* isomer: δ = –57.06 (dd, *J* = 7 and 12 Hz, 3 F, CF_3), –70.26 (dq, *J* = 6 and 12 Hz, 1 F, F^α) ppm. MS (EI): *m*/*z* = 263 $[M]^+$ (100%). $C_8H_5F_4N_5O$ (263.16): calcd. C 36.51, H 1.92, N 26.61; found C 36.82, H 2.07; N 26.22.

N^4-Benzoyl-N^1-(perfluoroprop-1-enyl)cytosine (9a): Compound **9** (430 mg, 2 mmol) gave **9a** (469 mg, 68% yield) as a colourless solid. M.p. 177–184 °C. ^{1}H NMR (300 MHz, $CDCl_3$ + CD_3OD, 25 °C): δ = 7.52–8.02 (m, 5 H, C_6H_5), 7.70 (m, 1 H, C^5–H), 7.81 (m, 1 H, C^6–H) ppm. ^{19}F NMR (282 MHz, $CDCl_3$ + CD_3OD, 25 °C): for *E* isomer: δ = –68.58 (dd, *J* = 11 and 21 Hz, 3 F, CF_3), –117.97 (dq, *J* = 21 and 132 Hz, 1 F, F^α), –164.04 (dq, *J* = 11 and 132 Hz, 1 F, F^β) ppm; for *Z* isomer: δ = –68.52 (m, 3 F, CF_3), –98.75 (m, 1 F, F^α), –152.91 (m,1 F, F^β) ppm. MS (EI): *m*/*z* = 345 $[M]^+$ (12%), 105 (100%). $C_{14}H_8F_5N_3O_2$ (345.24): calcd. C 48.71, H 2.34, N 12.17; found C 48.33, H 2.18, N 12.29.

N^6-Benzoyl-N^9-(perfluoroprop-1-enyl)adenine (10a): Compound **10** (478 mg, 2 mmol) gave unstable **10a** (89 mg, 12% yield) as a colourless solid. Unfortunately, **10a** undergoes a pretty fast decomposition. We were not able to get the absolutely pure compound for melting point determination and for elemental analysis even after a fine workup and a separation on preparative TLC plates. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.54–8.03 (m, 5 H,C_6H_5), 8.19 (s, 1 H, C^2–H), 8.86 (s, 1 H, C^8–H), 9.15 (br. s, 1 H,N^6–H) ppm. ^{19}F NMR (282 MHz, $CDCl_3$, 25 °C): for *E* isomer: δ = –68.20 (dd, *J* = 11 and 21 Hz, 3 F, CF_3), –118.58 (dq, *J* = 21 and 132 Hz, 1 F, F^α), –164.84 (dq, *J* = 11 and 132 Hz, 1 F, F^β) ppm; for *Z* isomer: δ = –68.28 (dd, *J* = 10 and 12 Hz, 3 F, CF_3), –94.99 (m, 1 F, F^α), –148.70 (m, 1 F, F^β) ppm. MS (EI): *m*/*z* = 369 $[M]^+$ (11%), 105 (100%).

N^4-Benzoyl-N^1,N^9-bis(perfluoroprop-1-enyl)adenine (12): Compound **10** (239 mg, 1 mmol and 4 molar excess of NaH) gave **12** (324 mg, 65% yield) as an oil. Compound **12** after certain period of time turns brown and undergoes a very slow decomposition. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.42–7.59 and 8.03–8.08 (m, 5 H, C_6H_5), 7.81 and 7.92 (m, 2 H, C^2–H and C^8–H) ppm. ^{19}F NMR (282 MHz, $CDCl_3$, 25 °C): δ = –67.93 [dd, *J* = 9 and 11 Hz, 3 F, (*Z*)-CF_3], –68.01 [dd, *J* = 8 and 11 Hz, 3 F, (*Z*)-CF_3], –68.23 to –68.56 [m, 6 F, (*E*)-CF_3], –94.94 [m, 1 F, (*Z*)-F^α], –98.35 [m, 1 F, (*Z*)-F^α], –117.04 [dm, *J* = 133 Hz, 1 F, (*E*)-F^α], –117.85 [dm, *J* = 133 Hz, 1 F, (*E*)-F^α], –148.11 [m, 1 F, (*Z*)-F^β], –149.66 [m, 1 F, (*Z*)-F^β], –161.70 [dm, *J* = 133 Hz, 1 F, (*E*)-F^β], –163.81 [dm, *J* = 133 Hz, 1 F, (*E*)-F^β] ppm. MS (EI): *m*/*z* = 499 $[M]^+$ (11%), 352 (43%), 105 (100%). $C_{18}H_7F_{10}N_5O$ (327.25): calcd. C 43.30, H 1.41, N 14.03; found C 42.94, H 1.79, N 13.79

N^4-Benzoyl-N^1-(1,3,3,3-tetrafluoroprop-1-enyl)cytosine (9b): Compound **9** (430 mg, 2 mmol) gave **9b** (582 mg, 89% yield) as a colour-

less solid. M.p. 196–198 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO, 25 °C): for *Z* isomer: δ = 6.56 (dq, *J* = 8 and 27 Hz, 1 H, H$^\beta$), 7.43 (m, 1 H, C^5–H), 7.50–8.00 (m, 5 H, C$_6$H$_5$), 8.30 (m, 1 H, C^6–H), 11.63 (br. s, 1 H, N^4–H) ppm; for *E* isomer: δ = 6.85 (m, 1 H, H$^\beta$), 7.43 (m, 1 H, C^5–H), 7.50–8.00 (m, 5 H, C$_6$H$_5$), 8.30 (m, 1 H, C^6–H), 11.65 (br. s, 1 H, N^4–H) ppm. ^{19}F NMR (282 MHz, [D$_6$]-DMSO, 25 °C): for *Z* isomer: δ = –56.58 (dd, *J* = 7 and 18 Hz, 3 F, CF$_3$), –78.48 (dq, *J* = 18 and 27 Hz, 1 F, F$^\alpha$) ppm; for *E* isomer: δ = –57.42 (dd, *J* = 7 and 12 Hz, 3 F, CF$_3$), –74.01 (dq, *J* = 6 and 12 Hz, 1 F, F$^\alpha$) ppm. MS (EI) for *Z* isomer: *m*/*z* = 327 [M]$^+$ (25%), 105 (100%). C$_{14}$H$_9$F$_4$N$_3$O$_2$ (327.25): calcd. C 51.38, H 2.77, N 12.84; found C 51.18, H 2.89, N 12.52.

N^6-Benzoyl-N^9-(1,3,3,3-tetrafluoroprop-1-enyl)adenine (10b): Compound **10** (478 mg, 2 mmol) gave **10b** (547 mg, 78% yield) as a colourless solid. M.p. 184–186 °C (for the *E* and *Z* mixture). ^{1}H NMR (300 MHz, CDCl$_3$, 25 °C): for *Z* isomer: δ = 6.81 (dq, *J* = 7 and 32 Hz, 1 H, H$^\beta$), 7.50–8.00 (m, 5 H, C$_6$H$_5$), 8.34 (s, 1 H, C^2–H), 8.90 (s, 1 H, C^8–H), 9.15 (br. s, 1 H, N^6–H) ppm; for *E* isomer: (CDCl$_3$ + CD$_3$OD, 25 °C): δ = 6.19 (dq, *J* = 6 and 7 Hz, 1 H, H$^\beta$), 7.50–8.10 (m, 5 H, C$_6$H$_5$), 8.25 (s, 1 H, C^2–H), 8.86 (s, 1 H, C^8–H) ppm. ^{19}F NMR (282 MHz, CDCl$_3$, 25 °C): for *Z* isomer: δ = –56.72 (dd, *J* = 7 and 18 Hz, 3 F, CF$_3$), –96.15 (dq, *J* = 18 and 32 Hz, 1 F, F$^\alpha$) ppm; for *E* isomer: (CDCl$_3$ + CD$_3$OD, 25 °C): δ = –58.58 (dd, *J* = 7 and 12 Hz, 3 F, CF$_3$), –74.14 (dq, *J* = 6 and 12 Hz, 1 F, F$^\alpha$) ppm. MS (EI) for *Z* isomer: *m*/*z* = 351 [M]$^+$ (6%), 105 (100%). MS (EI) for *E* isomer: *m*/*z* = 351 [M]$^+$ (14%), 105 (100%). Compound **10b** undergoes a slow decomposition, so we were not able to obtain the absolutely pure compound for elemental analysis.

N^4-Benzoyl-N^1-(2,3,3,3-tetrafluoro-1-iminopropyl)cytosine (11a) and N^4-Benzoyl-N^1-(2,3,3,3-tetrafluoropropanoyl)cytosine (11c): Compound **9a** (345 mg, 1 mmol) was dissolved in CH$_3$OH (10 mL), and a saturated solution of NH$_3$ in CH$_3$OH (10 mL) was added. After being stirred at room temperature overnight, the reaction mixture was concentrated under reduced pressure. The crude product was separated by column chromatography (silica gel, CH$_2$Cl$_2$, a gradient of CH$_2$Cl$_2$/CH$_3$OH) to give compound **11a** contaminated with a small amount of **11c** (223 mg).

Compound 11a: ^{1}H NMR (300 MHz, [D$_6$]DMSO, 25 °C): δ = 6.17 (dq, *J* = 7 and 44 Hz, 1 H, H$^\beta$), 6.25 (d, *J* = 13 Hz, 1 H, C^5–H), 7.59–7.76 and 7.95–8.04 (m, 5 H, C$_6$H$_5$), 8.67 (dq, *J* = 11 and 13 Hz, 1 H, C^6–H), 11.65 (d, *J* = 11Hz, 1 H, =N–H), 13.09 (br. s, 1 H, N^4–H) ppm. ^{19}F NMR (282 MHz, [D$_6$]DMSO, 25 °C): δ = –74.05 (dd, *J* = 7 and 12 Hz, 3 F, CF$_3$), –203.64 (dq, *J* = 12 and 44 Hz, 1 F, F$^\beta$) ppm. MS (EI): *m*/*z* = 342 [M]$^+$ (12%), 105 (100%), MS (FAB): *m*/*z* = 343 [M$^+$+1].

Compound 11c (as a Contaminant of 11a): ^{1}H NMR (300 MHz, [D$_6$]DMSO, 25 °C): δ = 5.64 (d, *J* = 9 Hz, 1 H, C^5–H), 6.38 (dm, *J* = 7 Hz, 1 H, H$^\beta$), 7.59–7.76 and 7.95–8.04 (m, 5 H, C$_6$H$_5$), 7.97 (d, *J* = 9 Hz, 1 H, C^6–H), 12.38 (br. s, 1 H, N^4–H) ppm. ^{19}F NMR (282 MHz, [D$_6$]DMSO, 25 °C): δ = –74.37 (dd, *J* = 7 and 11 Hz, 3 F, CF$_3$), –204.18 (m, 1 F, F$^\beta$) ppm.

Treatment of 2b with LiTMP/CD$_3$OD and *t*BuLi/CD$_3$OD and Characterization Data for Compounds 13–17: A solution of compound **2b** (56 mg, 0.25 mmol) in THF (1 mL) was added dropwise at –100 °C to a stirred solution of LiTMP (0.6 mmol) in anhydrous THF (10 mL), obtained from *n*BuLi (2.0 M) and TMP by a standard method,. The reaction mixture was kept for 10 min at this temperature, after which a solution of CD$_3$OD (2.2 mmol, 0.1 mL) in THF (0.5 mL) was added. This mixture was kept at the above temperature for an additional 30 minutes and was then allowed to warm to room temperature over a period of 2h. The solution was neutralized with methanolic HCl and concentrated to dryness under reduced pressure, and water (10 mL) was added. The aqueous solution was extracted with CH$_2$Cl$_2$ (2 × 20 mL) and the combined extracts were dried with Na$_2$SO$_4$. Solvent was removed, and the crude product was separated by column chromatography (silica gel, hexane, a gradient of hexane/CH$_2$Cl$_2$, CH$_2$Cl$_2$, a gradient of CH$_2$Cl$_2$/CH$_3$OH) to give compounds **13** and **16** contaminated with **17**.

The same procedure was applied for treatment of **2b** (56 mg, 0.25 mmol) with *t*BuLi (0.6 mmol) and CD$_3$OD (2.2 mmol, 0.1 mL) to give compounds **13**, **14** and **15**.

N^1-(2-Deuterio-1,3,3,3-tetrafluoroprop-1-enyl)uracil (13): This compound (6 mg, 11% yield) was obtained from the reaction with LiTMP/CD$_3$OD and also (5 mg, 9% yield) from the reaction with *t*BuLi/CD$_3$OD. M.p. 123–125 °C. ^{1}H NMR (300 MHz, CDCl$_3$, 25 °C): δ = 5.89 (d, *J* = 8 Hz, 1 H, C^5–H), 7.16 (d, *J* = 8 Hz, 1 H, C^6–H), 8.58 (br. s, 1 H, N^3–H) ppm. ^{19}F NMR (282 MHz, CDCl$_3$, 25 °C): δ = –59.7 (d, *J* = 12 Hz, 3 F, CF$_3$), –74.7 (q, *J* = 12 Hz, 1 F, F$^\alpha$) ppm. MS (EI): *m*/*z* = 225 [M]$^+$ (25%), 182 (100%). C$_7$H$_3$DF$_4$N$_2$O$_2$ (225.13): calcd. C 37.35, N 12.44; found C 37.05, N 12.12.

N^1-(1-*tert*-Butyl-3,3,3-trifluoroprop-1-enyl)uracil (14) and N^1-(1-*tert*-Butyl-2-deuterio-3,3,3-trifluoroprop-1-enyl)uracil (15): 32 mg (49% yield). M.p. 178–180 °C for **14**. ^{1}H NMR (300 MHz, CDCl$_3$, 25 °C): for **14**: δ = 1.30 (m, 9 H, *t*Bu), 5.76 (q, *J* = 7 Hz, 1 H, H$^\beta$), 5.83 (d, *J* = 8 Hz, 1 H, C^5–H), 7.06 (d, *J* = 8 Hz, 1 H, C^6–H), 9.30 (br. s, 1 H, N^3–H) ppm; for **15**: δ = 1.30 (m, 9 H, *t*Bu), 5.80 (m, 1 H, C^5–H), 7.00 (m, 1 H, C^6–H), 9.30 (br. s, 1 H, N^3–H) ppm. ^{19}F NMR (282 MHz, CDCl$_3$, 25 °C), for **14**: –60.27 (d, *J* = 7 Hz, 3 F, CF$_3$) ppm; for **15**: δ = –58.30 (s, 3 F, CF$_3$) ppm. MS (EI): *m*/*z* = 262 and 263 [M]$^+$ (32% and 44%), 206 and 205 (68% and 99%). C$_{11}$H$_{13}$F$_3$N$_2$O$_2$ (262.24) for **14**: calcd. C 50.38, H 5.00, N 10.68; found C 50.19, H 5.00, N 10.37.

N^1-(2-Deuterio-3,3,3-trifluoro-1-([D$_3$]methoxy)prop-1-enyl)uracil (16): 27 mg (45% yield). M.p. 116–118 °C. ^{1}H NMR (300 MHz, CDCl$_3$, 25 °C): δ = 5.87 (d, *J* = 8 Hz, 1 H, C^5–H), 7.28 (d, *J* = 8 Hz, 1 H, C^6–H), 9.08 (br. s, 1 H, N^3–H) ppm, together with traces of **17**: δ = 5.28 (q, *J* = 7 Hz, 1 H, H$^\beta$) ppm. ^{19}F NMR (282 MHz, CDCl$_3$, 25 °C): δ = –58.36 (s, 3 F, CF$_3$), together with traces of **17**: δ = –58.31 (d, *J* = 7 Hz, 3 F, CF$_3$) ppm. MS (EI): *m*/*z* = 240 [M]$^+$ (6%), 222 (100%). C$_8$H$_3$D$_4$F$_3$N$_2$O$_3$ (240.18): calcd. C 40.00, N 11.66; found C 40.29, N 11.39.

CCDC-653504 [compound (*Z*)-**9b**] contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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