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Article

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# Aza-Michael Access to Fluoroalkylidenes Analogues of Biomolecules

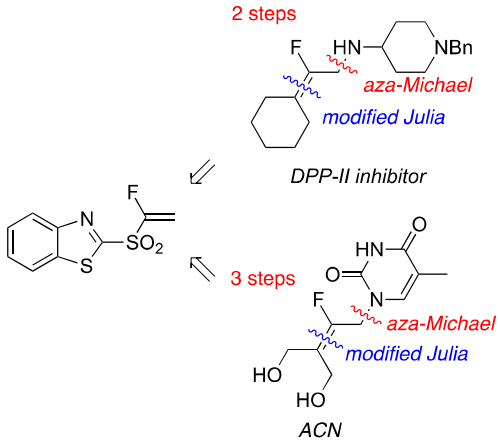
*Anaïs Prunier,*[†] *Charlène Calata,*[†] *Julien Legros,*[‡] *Jacques Maddaluno,*[‡] *Emmanuel Pfund,*[†] *Thierry Lequeux*[†]*

[†]Laboratoire de Chimie Moléculaire et Thioorganique, CNRS UMR 6507 & FR3038, Normandie Université, UNICAEN, ENSICAEN 6 Boulevard du Maréchal Juin, 14050 Caen Cedex, France

[‡]COBRA UMR 6014 CNRS & FR3038, INSA et Université de Rouen, 1 rue Tesnière, 76821 Mont Saint Aignan, France

*E-mail: Thierry.Lequeux@ensicaen.fr

***Graphical abstract***




**ABSTRACT**: The synthesis of fluoroaminosulfones derived from piperidine and nucleic bases, followed by the study of their chemical behaviour in the modified Julia reaction are described. The resulting aminosulfones open a straightforward access to a series of new fluorinated biomolecules including a potent DPP-II inhibitor, and acyclonucleoside analogues as potential enzyme inhibitors.

## INTRODUCTION

It is well established that the fluorovinylic moiety plays an increasingly important role in medicinal chemistry. When introduced onto nucleotides, carbohydrates, vitamins,

prostaglandins, steroids, and peptides it has been shown to improve their physiological stabilities or their biological activities.[1-3] Furthermore, Allmendinger's pioneer work on the structural analogy between an amide bond and a fluorinated carbon-carbon double bond,[4] has triggered interest on the effect of fluoroallylamines to prevent either rapid enzymatic degradation or natural isomerization occurring *in vivo* with peptides and their derivatives.[5-10] This last feature was already emphasized with the fluorinated PNA analogue **I**, as well as Dipeptidyl Peptidase (DPP) inhibitors **II** and **III**, in which increased activity was assigned to the fluoroalkene motif (Figure 1).[11-14] In the nucleoside field, a significant positive effect of the fluorovinylic moiety was also reported as exemplified by the potent antitumor fluorinated neplanocin A analogue **IV**,[15] and series of new fluorovinylic acyclic nucleosides (ACN) with anticancer properties.[16]

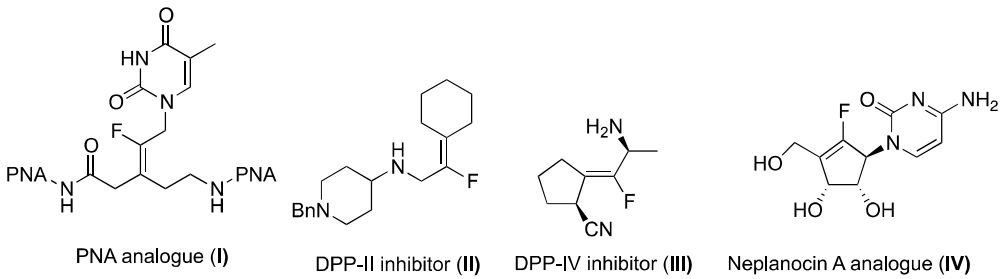
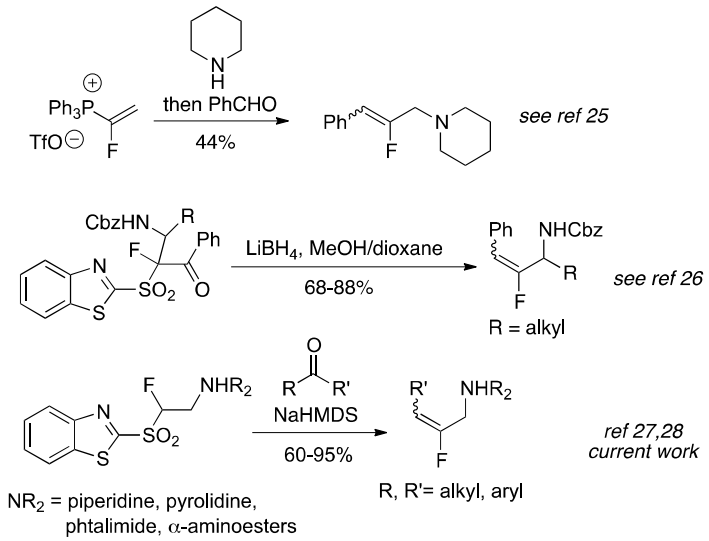



**Figure 1. Biologically Active Fluoroalkenes**

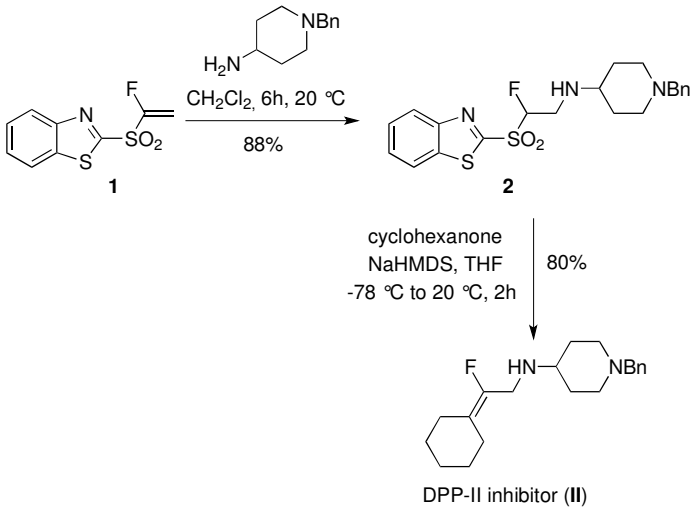
However, the access to functionalized fluoroallylamines, such as peptidomimetics or acyclo-nucleosides, is not straightforward. Most synthetic routes rely on the chemical modifications of α-fluoro-α,β-unsaturated esters. In general, these latters were prepared from the corresponding carbonyl compounds through Horner-Wadworth-Emmons, modified Julia, or Peterson reactions.[17-24] Up to date, the direct synthesis of fluoroallylamines can be achieved from aldehydes and piperidino-phosphonium ylide generated *in situ*,[25] by reduction of amino-fluoroketosulfones through a Smile rearrangement,[26] and recently *via* the modified Julia reaction between carbonyl compounds and fluoroaminosulfones (Scheme 1).[27,28] In this paper, we report the synthesis of aminosulfones by direct aza-Michael addition of functionalized amines and nucleic bases onto a fluorovinylsulfone, and a rapid access to important analogues of biomolecules including a DPP-II inhibitor and acyclonucleoside precursors.




**Scheme 1. Direct Routes for the Preparation of Fluoroallylamines**

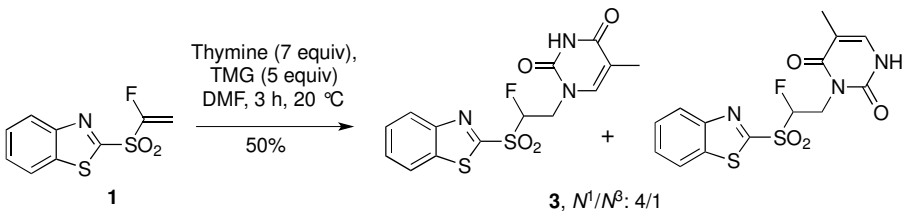
## RESULTS AND DISCUSSION

In connection with our previous results regarding the synthesis of fluoroallylamines,[28] the preparation of the DPP-II inhibitor **II** was first explored from the readily available benzothiazolylfluorovinylsulfone **1** (Scheme 2). While this inhibitor presents a good activity towards DPP-II,[13] its synthesis requires 6 steps from cyclohexanone. With a new tool for the synthesis of allylamines in hand, we explored a flexible and convergent preparation of this compound from piperidine derivatives. We recently reported an efficient conjugate addition of nucleophilic amines such as propylamine and cyclohexylamine onto fluorovinylsulfone **1**. This reaction proceeded smoothly in dichloromethane at 20 °C in a few minutes and afforded the corresponding aminosulfones in excellent yields.[27] The addition was found to be much slower when conducted with 4-amino-benzylpiperidine, and reached completion after 6 h of stirring at 20 °C in dichloromethane. Fluoroaminosulfone **2**, isolated in 88% yield, was next employed in the modified Julia reaction. A mixture of sulfone **2** and cyclohexanone (1.1 equiv) in THF was treated with NaHMDS (1.5 equiv) from -78 °C to 20 °C, and the fluoroallylamine **II** was obtained in 80% yield.



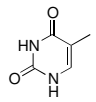
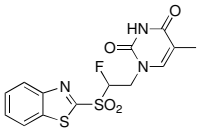
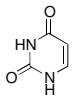
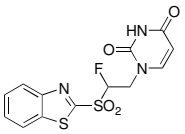
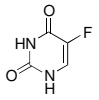
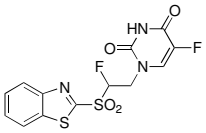
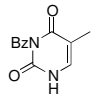
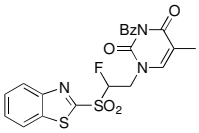
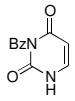
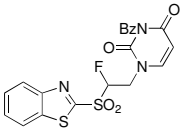
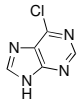
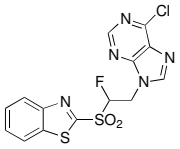
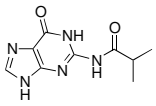
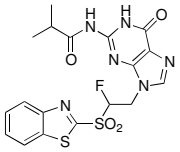

**Scheme 2. Two-step Synthesis of the DPP-II Inhibitor (II)**

This expeditious synthesis of DPP-II inhibitor **II** illustrates the efficiency of this approach, increasing the overall yield and the flexibility of compound **II** synthesis.[13] These results prompted us to apply a similar method to the preparation of fluorovinylic acyclonucleosides from sulfones bearing nucleic bases. However, the aza-Michael addition of nitrogen heterocycles is a challenging reaction that requires specific activation (e.g. high-pressure conditions).[29] Recently, Pathak reported the addition of heterocyclic amines, including nucleic bases, onto vinylic sulfones to afford the corresponding adducts in good yields when the reaction was performed in the presence of an excess of 1,1,3,3-tetramethylguanidine (TMG, 5 equiv) and amines (7 equiv).[30] Accordingly, the conjugate addition of nucleic bases was explored following Pathak's original procedure, and fluorovinylsulfone **1** was treated with thymine (7 equiv) in the presence of TMG (5 equiv). After 3 h of stirring at 20 °C in DMF, the reaction reached completion and the corresponding $N^1/N^3$ regioisomeric mixture of thymidyl fluorobenzothiazolylsulfone **3** was isolated in 50% yield in a 4:1 ratio. This medium yield is mainly due to difficulties to remove the excess of reagents from the reaction mixture (Scheme 3).




**Scheme 3. Conjugate Addition of Thymine onto Fluorovinylsulfone (1)**

**Table 1. Conjugate Addition of Nucleic Bases onto Fluorovinylsulfone (1)**

| Entry | Nucleic base | Product | Compound (Yield %)[a] |
|---|---|---|---|
| 1 |  |  | **3** (67%)[b] $N^1/N^3$: 4/1 |
| 2 |  |  | **4** (55%)[b] $N^1/N^3$: 9/1 |
| 3 |  |  | **5** (84%)[b] $N^1/N^3$: 100/0 |
| 4 |  |  | **6** (95%)[b] |
| 5 |  |  | **7** (84%)[b] |
| 6 |  |  | **8** (74%)[c] $N^7/N^9$: 0/100 |
| 7 |  |  | **9** (73%)[c] $N^7/N^9$: 2/3 |

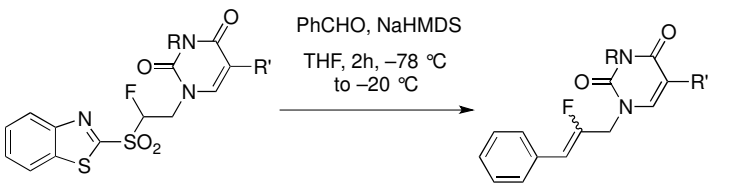
[a] Isolated yield; [b] Nucleic base (1.3 equiv), TBAF (0.2 equiv), THF, 20 °C, 16 h;

[c] Nucleic base (1.1 equiv), TBAF (0.2 equiv), DMF, 20 °C, 24 h.

Other catalysts were explored, such as tetrabutylammonium fluoride (TBAF). This reagent has been used for a variety of base-catalyzed reactions,[31] including Michael addition,[32,33] and we already reported that TBAF enhances the reactivity of nitrogen nucleophiles such as phtalimide.[27] Addition of thymine onto vinylsulfone **1** was performed in the presence of TBAF in THF. Best results were obtained when the aza-Michael reaction was conducted over 16 h at 20 °C in the presence of 20 mol% of catalyst. The fluorinated thymine derivative **3** was obtained in 67% yield as a 4:1 mixture of $N^1$ and $N^3$ isomers. This reaction was extended to other protected and unprotected nucleic bases (Table 1).

The conjugate addition of unprotected uracil gave roughly the same results than those obtained from thymine, and sulfonyl-uracil derivative **4** was isolated in 55% yield as a mixture of both $N^1$ and $N^3$ regioisomers (Table 1, entry 2). In contrast, from 5-fluorouracil, the $N^1$ isomer was exclusively detected and benzothiazolylfluorosulfone **5** was isolated in 84% yield (Table 1, entry 3). In this case, the presence of the fluorine atom onto the nucleic base decreased the $N^3$ atom nucleophilicity leading to the exclusive alkylation of the $N^1$ position. To prevent the formation of the undesired $N^3$ alkylated thymine and uracil derivatives, the aza-Michael reaction was conducted from their corresponding $N^3$-benzoylated derivatives. The protected fluorosulfonyl-thymine and -uracil **6**, **7** were prepared in good yields, and the protecting group survived the reaction conditions (Table 1, entries 4 and 5). These mild conditions were then applied to the purine series. To overcome the poor solubility of purines, DMF was preferred to THF as solvent. From 6-chloropurine, the conjugate addition reaction was slower and the reaction reached completion after 24 h of stirring at 20 °C. Fluorosulfonyl 6-chloropurine **8** was isolated in 74% yield as a single isomer (Table 1, entry 6). In contrast, a non separable mixture of both $N^7$ and $N^9$ regioisomers **9** was obtained when the aza-Michael reaction was conducted with $N^2$-(isobutanoyl)-guanine (Table 1, entry 7).

The chemical behaviours of these fluorosulfones in the modified Julia reaction was next investigated in an attempt to access fluorovinylic acyclonucleosides. The reactivity of pyrimidinyl sulfones **6, 7** was first evaluated with benzaldehyde in the presence of NaHMDS (1.5 equiv) in THF (Scheme 4). After stirring for 30 min at –78 °C, the mixture was maintained 1.5 h at –20 °C to avoid the debenzoylation of the heterocycle. Fluoroalkylidene derivatives **11, 12** were obtained in good yields (69–87%), and a high *Z* selectivity (*Z*/*E* > 9:1, Scheme 4). In the presence of *t*BuOK, similar selectivities were observed, but the yield tumbled down to 45%. We noticed this selectivity was depended strongly on the presence of the $N^3$-benzoyl group onto the nucleic base. Indeed, a 1:1 mixture of both *Z*/*E* isomers **13** was obtained from **5**.

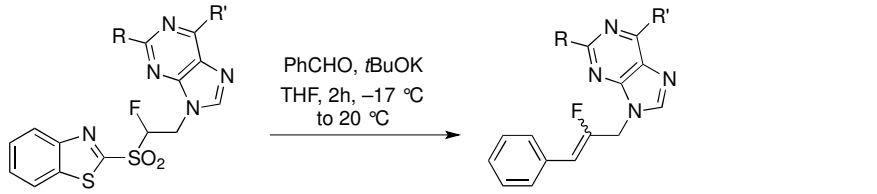



**6**, R = Bz, R' = $CH_3$
**7**, R = Bz, R' = H
**5**, R = H, R' = F
**10**, R = Bz, R' = F

**11**, R = Bz, R' = $CH_3$, *E*/*Z* = 5:95, 87%
**12**, R = Bz, R' = H, *E*/*Z* = 6:94, 69%
**13**, R = H, R' = F, *E*/*Z* = 47:53, 69%
**14**, R = Bz, R' = F, *E*/*Z* = 5:95, 39%

**Scheme 4. Fluoroolefination Reaction of Benzaldehyde with Pyrimidinyl Fluorosulfones**

In contrast, when the reaction was achieved with the corresponding protected sulfone **10**,[34] once again the *Z* isomer **14** was obtained as the major product (*Z*/*E* > 9:1). Surprisingly, when applied to the more sensitive purine series (sulfones **8** and **9**), the reaction afforded a mixture of unidentified products. A clean reaction was observed when *t*BuOK was used as base instead of NaHMDS. In these cases, corresponding fluoroalkenes **15** and **16** were isolated in 61% and 55% yield, respectively, but without any selectivity (Scheme 5). These results suggest that the steric hindrance of the nucleic bases is not the only parameter controlling the selective formation of the carbon-carbon double bond.

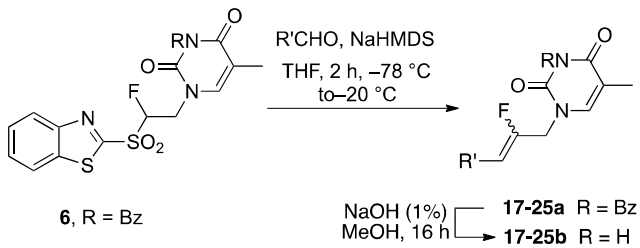



**8**, R = H, R' = Cl
**9**, R = NHC(O)CH(CH$_3$)$_2$, R' = OH

**15**, R = H, R' = Cl, *E*/*Z* = 55:45, 61%
**16**, R = NHC(O)CH(CH$_3$)$_2$, R' = OH, *E*/*Z* = 2:3, 55%

**Scheme 5. Fluoroolefination Reaction of Benzaldehyde with Purinyl Fluorosulfones**

To approach acyclic structures related to precursors of acyclonucleosides such as thymidine nucleoside phosphorylase (TPase) inhibitors,[35] the olefination of a series of carbonyl compounds was explored with the fluorosulfone **6**. It has been shown that alkylated nucleic bases would be good candidates, and the presence of a heterocycle or an aromatic ring influenced strongly the inhibition activity towards nucleoside phosphorylases.[36,37] In a first instance, the synthesis of aromatic derivatives, as potential non-ionic TPase inhibitor analogues, was performed from sulfone **6** and aldehydes (Scheme 6, Table 2).

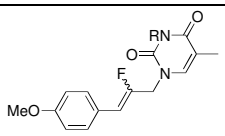
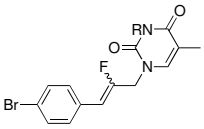
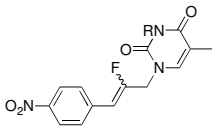
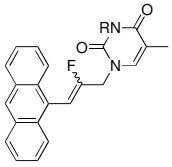
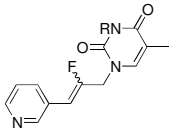
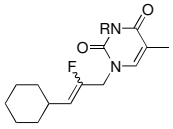
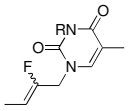
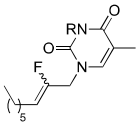
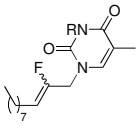



**6**, R = Bz

**17-25a** R = Bz
**17-25b** R = H

**Scheme 6. Synthesis of Fluoroallylthymine Derivatives.**

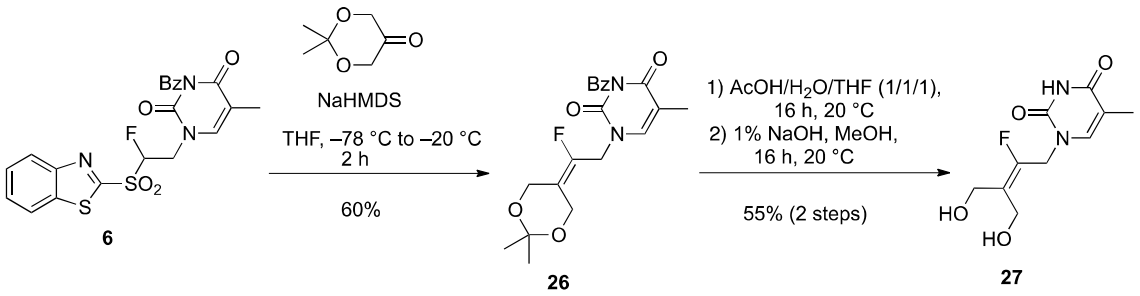
**Table 2. Fluoroolefination Reaction of Aldehydes with Fluorosulfone (6)**

| Entry | Aldehyde | Product | R = Bz (Yield, *E/Z*)[a] | R = H (Yield, *E/Z*)[b] |
|---|---|---|---|---|
| 1 | 4-MeO-PhCHO |  | **17a** (79%, 4:96) | **17b** (76%, 7:93) |
| 2 | 4-Br-PhCHO |  | **18a** (86%, 8:92) | **18b** (55%, 17:83) |
| 3 | 4-$NO_2$-PhCHO |  | **19a** (63%, 32:68) | - |
| 4 | $Ph_3CHO$ |  | **20a** (82%, 17:83) | **20b** (65%, 15:85) |
| 5 | $C_5H_4N$-CHO |  | **21a** (61%, 16:84) | **21b** (66%, 12:88) |
| 6 | $C_6H_{11}CHO$ |  | **22a** (83%, 28:72) | **22b** (57%, 21:79) |
| 7 | MeCHO |  | **23a** (88%, 41:59) | **23b** (82%, 39:61) |
| 8 | $CH_3(CH_2)_5CHO$ |  | **24a** (61%, 29:71) | **24b** (67%, 30:70) |
| 9 | $CH_3(CH_2)_7CHO$ |  | **25a** (52%, 30:70) | **25b** (78%, 28:72) |

[a] *E/Z* ratio in the crude mixture determined by $^{19}F$ NMR. [b] Yield after 2 steps including modified Julia reaction followed by thymine deprotection using 1% NaOH in MeOH.

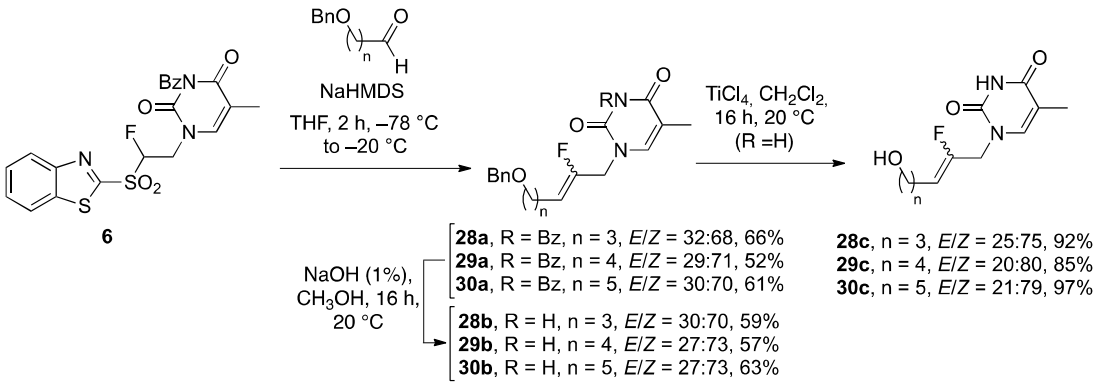
From aromatic aldehydes bearing a *para* electron-donating substituent such as a methoxy group or a bromine atom, corresponding fluoroalkenes derived from thymine **17–18a** were formed with a high *Z*-selectivity after 2 h of stirring, and the expected products were isolated in 71–76% yields (Table 2, entries 1, 2). The presence of an electron-withdrawing substituent on the aromatic ring did not alter the reaction efficiency and compound **19a** was obtained also in good yield (Table 2, entry 3). The reaction carried out with anthraldehyde and 3-pyridinecarboxaldehyde furnished fluoroolefins **20–21a** in 61–82% yields, and the *Z*-selectivities were preserved (Table 2, entries 4, 5). From aliphatic aldehydes such as cyclohexylcarboxaldehyde, the olefination reaction was faster and reached completion after 30 min of stirring. The corresponding 3-benzoylthyminyl derivative **22a** was isolated in 83% yield, but the *Z*-selectivity was slightly altered (Table 2, entry 6). Applied to a series of linear aliphatic aldehydes the reaction afforded compounds **23–25a** in moderate to good yields, and *Z* alkenes were formed as major products (Table 2, entries 7, 8, 9). While excellent yield was obtained from acetaldehyde, isolated yields gradually decreased from heptanal to nonanal. For these latters, partial deprotection of the thymine occurred during the olefination process. A two-step process was carried out by treatment of the crude mixture of alkenes with NaOH (1%) in $CH_3OH$ (Scheme 6), as exemplified by the preparation of compound **25b** isolated in 78% overall yield (Table 2, entry 9), and the other compounds of the series (compounds **17-18b, 20–24b**). This additional step increased the overall yields without alterating the selectivity of the modified Julia reaction.

This approach was applied to polyhydroxylated carbonyl compounds in an attempt to open a new access to analogues of acyclonucleosides. It has been reported that the *trans*-butenyl moiety could mimic the conformation of the $C_{1'}$-$O_{4'}$-$C_{4'}$-$C_{5'}$ atoms of the natural 2-deoxyribose (dUMP).[38-40] Due to the highest electronegative character of the fluorine atom, fluoroalkene moiety could enhance this feature better than an alkene. This prompted us to carry out the olefination of polyhydroxylated carbonyl compounds (Scheme 7). To start with the synthesis of the closest analogue of the *trans*-butenyl moiety, 1,3-isopropylidene acetone was considered as a fine partner. The modified Julia reaction was run with sulfone **6** and 1,3-isopropylidene acetone. By treatment of **6** and the ketone with NaHDMS in THF, we were pleased to observe the formation of the expected alkene **26**. After work-up and purification by flash chromatography, compound **26** was isolated in 60% yield. Finally, acetal hydrolysis followed by thymine deprotection according to a standard protocol furnished the fluorinated *trans*-butenyl **27** in good overall yield.




**Scheme 7. Preparation of a Fluorinated Analogue of Acyclonucleosides.**

To extend this synthesis to other series containing larger spacers between the hydroxyl function and the nucleic base,[41] the reaction was carried out from alkoxyaldehydes. While $\tilde{\alpha}$ and $\tilde{\beta}$benzyloxyaldehydes, such as benzyloxyacetaldehyde and 3-benzyloxypropanal, failed to react with **6**, $\tilde{\gamma}$, $\tilde{\delta}$, and $\tilde{\omega}$alkoxyaldehydes afforded the corresponding alkenes in moderate yields (Scheme 8). From 4-benzyloxybutanal, 5-benzyloxypentanal and 6-benzyloxyhexanal the reaction reached completion in the presence of NaHMDS, after stirring for 30 min at -78 °C and 1.5 h at -20 °C. In these cases, thymine deprotection did not occurred, and the corresponding acyclonucleosides **28-30a** were isolated in 52-66% yields. Although the *Z* isomer was the major product of the reaction, an inseparable mixture of both *E*/*Z* isomers was obtained. Finally, corresponding fluoroallylthymines derivatives **28-30c** were obtained after treatment with NaOH (1%) in MeOH followed by a selective debenzylation with $TiCl_4$ (5 equiv) in methylene chloride.[42,43]




**Scheme 8. Fluoroolefination Reaction of Functionalized Aldehydes with Sulfone (6)**

## CONCLUSION

In summary, the chemical behavior of a large variety of benzothiazolylfluoroaminosulfones in the modified Julia reaction was reported. Fluorinated aminosulfone **2**, easily obtained by conjugate addition of 4-benzylamino-piperidine onto benzothiazolyl-fluorovinylsulfone **1**, appeared as an efficient fluoroolefination reagent to carry out a straightforward and flexible synthesis of a potent DPP-II inhibitor. The synthesis of modified acyclonucleoside precursors was explored from a series of new fluoroaminosulfones containing pyrimidine and purine heterocycles. The modified Julia reaction was highly *Z*-selective from benzoylated thymidinylsulfones and aromatic as well as aliphatic aldehydes, and corresponding acyclonucleoside precursors were isolated in moderate to good yields. Biological evaluation of these compounds as Thymidine Phosphorylase inhibitors and antiviral agents are in progress and results will be reported in due course. To conclude, these examples illustrated the efficiency of the modified Julia reaction, appearing as a convenient tool for the convergent synthesis of highly functionalized fluoroalkylidenes.

## EXPERIMENTAL SECTION

**General.** All commercially available reagents were bought and used as received. For anhydrous conditions, the glassware was flamed under a continuous nitrogen flow and cooled to 20 °C before running the experiment. Anhydrous solvents (THF, $CH_2Cl_2$, $CH_3CN$ and Toluene) were dried in a solvent generator, which uses an activated alumina column to remove water. DMF, $Et_3N$ and pyridine were distilled under $CaH_2$ or 4 Å molecular sieves. Flash column chromatography was realized on silica gel 60 (40-63 μm) with air pressure and products were detected by thin layer chromatography, on which the spots were visualized by UV-irradiation and/or $KMnO_4$ solution. NMR spectra were recorded on a 400 MHz or 500 MHz apparatus in deutered solvent at 25 °C. All chemical shifts are reported in δ parts per million (ppm) and coupling constants (*J*) are in hertz (Hz). The following abbreviations mean: s: singlet; d: doublet; t triplet; q: quadruplet; quint: quintuplet; sext: sextet; sep: septet; m: multiplet. High-resolution mass data were recorded on a Micromass Q-TOF (Quadrupole Time-of-Flight) instrument with an electrospray source in the EI or ESI mode.

***N*-[2-(1,3-Benzothiazole-2-sulfonyl)-2-fluoroethyl]-1-benzylpiperidin-4-amine (2).** To a solution of 2-(1-fluoroethenesulfonyl)-1,3-benzothiazole **1**[27] (200 mg, 0.82 mmol, 1 equiv) in $CH_2Cl_2$ (4 mL) was added 4-amino-1-benzylpiperidine (0.22 mL, 1.07 mmol, 1.3 equiv). The mixture was stirred for 6 h at 20 °C then quenched with a saturated aqueous solution of

$NH_4Cl$ (2 mL). The aqueous layer was extracted with $CH_2Cl_2$ (3 x 8 mL). The combined organic layers were dried over $MgSO_4$, filtered and evaporated under reduced pressure. The crude product was purified by flash column chromatography ($CH_2Cl_2$/MeOH, 95:5) to give aminosulfone **2** (314 mg, 88%) as a yellow oil. $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 8.22–8.20 (m, 1H), 7.98–7.95 (m, 1H), 7.62–7.54 (m, 2H), 7.27–7.25 (m, 4H), 7.23–7.19 (m, 1H), 5.72 (ddd, $^2J_{HF}$ = 46.5 Hz, $^3J_{HH}$ = 7.5 Hz, $^3J_{HH}$ = 3.6 Hz, 1H), 3.56–3.32 (m, 2H), 3.44 (s, 2H), 2.79–2.76 (m, 2H), 2.54–2.47 (m, 1H), 1.98 (t, $^3J_{HH}$ = 10.3 Hz, 2H), 1.79–1.76 (m, 2H), 1.69 (sbr, 1H), 1.40–1.29 (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 162.4, 152.6, 138.1, 137.2, 128.9 (2C), 128.3, 128.0 (2C), 127.7, 126.8, 125.6, 122.2, 101.4 (d, $^1J_{CF}$ = 223.3 Hz), 62.7, 54.2, 51.8 (2C), 43.4 (d, $^2J_{CF}$ = 20.0 Hz), 32.3, 32.1; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –181.1 (ddd, $^2J_{FH}$ = 46.5 Hz, $^3J_{FH}$ = 27.9 Hz, $^3J_{FH}$ = 18.3 Hz, 1F); MS (ESI) *m/z* 434 $[M + H]^+$ (12), 174 (100), 91 (11); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{21}H_{25}FN_3O_2S_2$ 434.1372, found 434.1375.

**1-Benzyl-*N*-(2-cyclohexylidene-2-fluoroethyl)piperidin-4-amine (II).** To a solution of aminosulfone **2** (80 mg, 0.18 mmol, 1 equiv), and cyclohexanone (21 μL, 0.20 mmol, 1.1 equiv) at –78 °C in THF (2 mL) was added NaHMDS (1 M in THF, 0.28 mL, 0.28 mmol, 1.5 equiv). After 30 min at –78 °C, the mixture was stirred for 1 h 30 at 20 °C, quenched with a saturated aqueous solution of $NH_4Cl$ (1 mL) and extracted with $CH_2Cl_2$ (3 x 5 mL). Combined organic layers were washed with brine, dried over $MgSO_4$, filtered and evaporated under reduced pressure. The crude product was purified by flash column chromatography ($CH_2Cl_2$/MeOH, 9:1) to give amino-alkene **II** (47 mg, 80%) as a yellow oil. $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.28–7.22 (m, 4H), 7.20–7.16 (m, 1H), 3.47 (s, 2H), 3.36 (d, $^3J_{HF}$ = 22.1 Hz, 2H), 2.83–2.78 (m, 2H), 2.50–2.44 (m, 1H), 2.15 (m, 2H), 2.04–1.99 (m, 4H), 1.79–1.76 (m, 2H), 1.46–1.45 (m, 6H), 1.41–1.35 (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 149.2 (d, $^1J_{CF}$ = 241.8 Hz), 137.9, 129.1 (2C), 128.1 (2C), 127.0, 118.3 (d, $^2J_{CF}$ = 15.2 Hz), 62.8, 52.9, 51.9 (2C), 42.7 (d, $^2J_{CF}$ = 30.3 Hz), 32.1 (2C), 28.2 (d, $^3J_{CF}$ = 5.1 Hz), 27.6 (d, $^4J_{CF}$ = 2.5 Hz), 26.8, 26.3, 25.5 (d, $^3J_{CF}$ = 8.4 Hz); $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –121.3 (t, $^3J_{FH}$ = 22.1 Hz, 1F); MS (ESI) *m/z* 317 $[M + H]^+$ (32), 174 (100); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{20}H_{30}FN_2$ 317.2393, found 317.2393.

**General procedure A: conjugate addition of nucleic bases (pyrimidine series) onto fluorovinylsulfone.** To a solution of nucleic base (1.3 equiv) in THF (0.2 M) were added TBAF (1 M in THF, 0.2 equiv) and 2-(1-fluoroethenesulfonyl)-1,3-benzothiazole **1** (1 equiv). The mixture was stirred for 16 h at 20 °C, quenched with a saturated aqueous solution of $NH_4Cl$ and extracted with $CH_2Cl_2$. Combined organic layers were dried over $MgSO_4$, filtered

and evaporated under reduced pressure. The crude product was purified by flash column chromatography or by filtration to give fluorinated aminosulfones **3-7**.

**1-[2-(1,3-Benzothiazole-2-sulfonyl)-2-fluoroethyl]-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (3).** General procedure A was followed with sulfone **1** (100 mg, 0.41 mmol, 1 equiv), thymine (63 mg, 0.53 mmol, 1.3 equiv) and TBAF (1 M in THF, 82 µL, 0.08 mmol, 0.2 equiv) in THF (2 mL). The purification by flash chromatography ($CH_2Cl_2$/AcOEt, 9:1 then 8:2) afforded compound **3** as a mixture of regioisomers ($N^1/N^3$, 4:1) as a white solid (102 mg, 67%). Mp 205 °C; $^1$H NMR (DMSO, 400 MHz) $\delta$ 11.44 (s, 1H, $N^1$-isomer), 11.12 (s, 1H, $N^3$-isomer), 8.40–8.38 (m, 2H, $N^1$ and $N^3$-isomers), 8.35–8.33 (m, 2H, $N^1$ and $N^3$-isomers), 7.77–7.75 (m, 4H, $N^1$ and $N^3$-isomers), 7.53 (s, 1H, $N^1$-isomer), 7.34 (s, 1H, $N^3$-isomer), 6.46 (ddd, $^2J_{HF}$ = 46.7 Hz, $^3J_{HH}$ = 6.0 Hz, $^3J_{HH}$ = 1.8 Hz, 1H, $N^1$-isomer), 6.45 (ddd, $^2J_{HF}$ = 46.7 Hz, $^3J_{HH}$ = 6.0 Hz, $^3J_{HH}$ = 1.8 Hz, 1H, $N^3$-isomer), 4.70–4.59 (m, 2H, $N^1$ and $N^3$-isomers), 4.41–4.32 (m, 2H, $N^1$ and $N^3$-isomers), 1.76 (s, 3H, $N^3$-isomer), 1.72 (s, 3H, $N^1$-isomer); $^{13}$C NMR (DMSO, 125 MHz) $N^3$-isomer $\delta$ 164.1, 161.7, 152.3, 150.8, 141.0, 137.2, 128.9, 128.4, 125.4, 123.7, 109.2, 99.2 (d, $^1J_{CF}$ = 222.4 Hz), 44.7 (d, $^2J_{CF}$ = 20.7 Hz), 11.9; $^{19}$F NMR (DMSO, 376 MHz) $\delta$ –183.6 (ddd, $^2J_{FH}$ = 46.7 Hz, $^3J_{FH}$ = 33.8 Hz, $^3J_{FH}$ = 12.8 Hz, 1F, $N^3$-isomer), –183.8 (ddd, $^2J_{FH}$ = 46.7 Hz, $^3J_{FH}$ = 30.8 Hz, $^3J_{FH}$ = 15.8 Hz, 1F, $N^1$-isomer); MS (ESI) *m/z* 370 $[M + H]^+$ (95), 171 (100); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{14}H_{13}FN_3O_4S_2$ 370.0335, found 370.0332.

**1-[2-(1,3-Benzothiazole-2-sulfonyl)-2-fluoroethyl]-1,2,3,4-tetrahydropyrimidine-2,4-dione (4).** General procedure A was followed with sulfone **1** (100 mg, 0.41 mmol, 1 equiv), uracil (60 mg, 0.53 mmol, 1.3 equiv) and TBAF (1 M in THF, 82 µL, 0.08 mmol, 0.2 equiv) in THF (2 mL). The purification by flash chromatography ($CH_2Cl_2$/AcOEt 1:1) afforded compound **4** as a mixture of regioisomers ($N^1/N^3$, 9:1) as a white solid (53 mg, 55%). Mp 190 °C; $^1$H NMR (DMSO, 400 MHz) $\delta$ 11.45 (s, 1H, $N^1$-isomer), 11.34 (s, 1H, $N^3$-isomer), 8.42–8.32 (m, 4H, $N^1$ and $N^3$-isomers), 7.79–7.73 (m, 4H, $N^1$ and $N^3$-isomers), 7.65 (d, $^3J_{HH}$ = 7.9 Hz, 1H, $N^1$-isomer), 7.48 (d, $^3J_{HH}$ = 7.6 Hz, 1H, $N^3$-isomer), 6.47 (ddd, $^3J_{HF}$ = 46.6 Hz, $^2J_{HH}$ = 8.1 Hz, $^3J_{HH}$ = 2.7 Hz, 1H, $N^1$-isomer), 6.30 (ddd, $^3J_{HF}$ = 46.9 Hz, $^2J_{HH}$ = 8.4 Hz, $^3J_{HH}$ = 2.7 Hz, 1H, $N^3$-isomer), 5.63 (d, $^3J_{HH}$ = 7.6 Hz, 1H, $N^3$-isomer), 5.61 (d, $^3J_{HH}$ = 7.9 Hz, 1H, $N^1$-isomer), 4.74–4.36 (m, 4H, $N^1$ and $N^3$-isomer); $^{13}$C NMR (DMSO, 100 MHz) $\delta$ 163.6 ($N^1$-isomer), 162.8 ($N^3$-isomer), 161.9 ($N^3$-isomer), 161.7 ($N^1$-isomer), 152.3 (2C, $N^1$ and $N^3$-isomers), 151.2 ($N^3$-isomer), 150.8 ($N^1$-isomer), 145.4 ($N^1$-isomer), 141.5 ($N^3$-isomer), 137.2 ($N^1$-isomer), 137.1 ($N^3$-isomer), 128.9 (2C, $N^1$ and $N^3$-isomers), 128.4 (2C, $N^1$ and $N^3$-isomer), 125.4 (2C, $N^1$ and $N^3$-isomer), 123.7 (2C, $N^1$ and $N^3$-isomer), 101.7 ($N^1$-isomer), 99.6 ($N^3$-

isomer), 99.1 (d, $^{1}J_{CF}$ = 222.2 Hz, $N^{1}$-isomer), 98.7 (d, $^{1}J_{CF}$ = 223.9 Hz, $N^{3}$-isomer), 44.9 (d, $^{2}J_{CF}$ = 20.5 Hz, $N^{1}$-isomer) 37.2 (d, $^{2}J_{CF}$ = 20.5 Hz, $N^{3}$-isomer); $^{19}$F NMR (DMSO, 376 MHz) $\delta$ –183.3 (ddd, $^{2}J_{FH}$ = 46.9 Hz, $^{3}J_{FH}$ = 33.1 Hz, $^{3}J_{FH}$ = 14.5 Hz, 1F, $N^{3}$-isomer), –183.6 (ddd, $^{2}J_{FH}$ = 46.6 Hz, $^{3}J_{FH}$ = 30.5 Hz, $^{3}J_{FH}$ = 16.1 Hz, 1F, $N^{1}$-isomer); HRMS (ESI) *m/z* $[M + Na]^{+}$ calcd for $C_{13}H_{10}FN_3NaO_4S_2$ 377.9994, found 377.9995.

**1-[2-(1,3-Benzothiazole-2-sulfonyl)-2-fluoroethyl]-5-fluoro-1,2,3,4-tetrahydropyrimidine-2,4-dione (5)**. General procedure A was followed with sulfone **1** (100 mg, 0.41 mmol, 1 equiv), 5-fluorouracil (70 mg, 0.53 mmol, 1.3 equiv) and TBAF (1 M in THF, 82 µL, 0.08 mmol, 0.2 equiv) in THF (2 mL). The $CH_2Cl_2$ was added to the crude product and the pure solid compound **5** was recovered by filtration (129 mg, 84%) as a white solid. Mp 225 °C; $^{1}$H NMR (DMSO, 400 MHz) $\delta$ 11.99 (s, 1H), 8.44–8.40 (m, 1H), 8.38–8.34 (m, 1H), 8.11 (d, $^{3}J_{HF}$ = 6.7 Hz, 1H), 7.82–7.75 (m, 2H), 6.46 (ddd, $^{2}J_{HF}$ = 46.6 Hz, $^{3}J_{HH}$ = 8.4 Hz, $^{3}J_{HH}$ = 2.7 Hz, 1H), 4.64 (ddd, $^{3}J_{HF}$ = 31.1 Hz, $^{2}J_{HH}$ = 15.2 Hz, $^{3}J_{HH}$ = 2.7 Hz, 1H), 4.35 (ddd, $^{3}J_{HF}$ = 15.7 Hz, $^{2}J_{HH}$ = 15.2 Hz, $^{3}J_{HH}$ = 8.4 Hz, 1H); $^{13}$C NMR (DMSO, 100 MHz) $\delta$ 161.6, 157.3 (d, $^{2}J_{CF}$ = 25.9 Hz), 152.3, 149.5, 139.6 (d, $^{1}J_{CF}$ = 229.9 Hz), 137.2, 129.8 (d, $^{2}J_{CF}$ = 34.6 Hz), 128.9, 128.4, 125.4, 123.7, 99.0 (d, $^{1}J_{CF}$ = 222.9 Hz), 45.0 (d, $^{2}J_{CF}$ = 20.6 Hz); $^{19}$F NMR (DMSO, 376 MHz) $\delta$ –169.0 (d, $^{3}J_{FH}$ = 6.7 Hz, 1F), –183.7 (ddd, $^{2}J_{FH}$ = 46.6 Hz, $^{3}J_{FH}$ = 31.1 Hz, $^{3}J_{FH}$ = 15.7 Hz, 1F); MS (ESI) *m/z* 374 $[M + H]^{+}$ (72), 175 (100), 136 (36); HRMS (ESI) *m/z* $[M + H]^{+}$ calcd for $C_{13}H_{10}F_2N_3O_4S_2$ 374.0081, found 374.0082.

**3-Benzoyl-1-[2-(1,3-benzothiazole-2-sulfonyl)-2-fluoroethyl]-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (6).** General procedure A was followed with sulfone **1** (2.0 g, 8.22 mmol, 1 equiv), $N^{3}$-benzoylthymine (2.46 g, 10.69 mmol, 1.3 equiv) and TBAF (1 M in THF, 1.6 mL, 1.64 mmol, 0.2 equiv) in THF (40 mL). The purification by flash chromatography ($CH_2Cl_2$/AcOEt, 95:5) afforded compound **6** (3.73 g, 95%) as a white solid. Mp 88 °C; $^{1}$H NMR ($CDCl_3$, 400 MHz) $\delta$ 8.27–8.25 (m, 1H), 8.05–8.03 (m, 1H), 7.94–7.91 (m, 2H), 7.70–7.62 (m, 3H), 7.51–7.47 (m, 2H), 7.20 (s, 1H), 6.04 (ddd, $^{2}J_{HF}$ = 47.7 Hz, $^{3}J_{HH}$ = 7.6 Hz, $^{3}J_{HH}$ = 4.5 Hz, 1H), 4.77 (ddd, $^{3}J_{HF}$ = 23.3 Hz, $^{2}J_{HH}$ = 15.0 Hz, $^{3}J_{HH}$ = 4.5 Hz, 1H), 4.35 (ddd, $^{3}J_{HF}$ = 11.9 Hz, $^{2}J_{HH}$ = 15.0 Hz, $^{3}J_{HH}$ = 7.6 Hz, 1H), 1.96 (d, $^{3}J_{HH}$ = 1.2 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.3, 162.8, 161.1, 152.7, 149.7, 140.1, 137.4, 135.2, 131.2, 130.4 (2C), 129.2 (2C), 128.8, 128.1, 126.0, 122.4, 111.7, 97.4 (d, $^{1}J_{CF}$ = 225.4 Hz), 46.6 (d, $^{2}J_{CF}$ = 22.6 Hz), 12.3; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –182.4 (ddd, $^{2}J_{FH}$ = 47.7 Hz, $^{3}J_{FH}$ = 23.3 Hz, $^{3}J_{FH}$ = 11.9 Hz, 1F); MS (ESI) *m/z* 474 $[M + H]^{+}$ (80), 105 (100); HRMS (ESI) *m/z* $[M + H]^{+}$ calcd for $C_{21}H_{17}FN_3O_5S_2$ 474.0594, found 474.0601.

**3-Benzoyl-1-[2-(1,3-benzothiazole-2-sulfonyl)-2-fluoroethyl]-1,2,3,4-tetrahydropyrimidine-2,4-dione (7).** General procedure A was followed with sulfone **1** (100 mg, 0.41 mmol, 1 equiv), $N^3$-benzoyluracil (116 mg, 0.53 mmol, 1.3 equiv) and TBAF (1 M in THF, 82 µL, 0.08 mmol, 0.2 equiv) in THF (2 mL). The purification by flash chromatography ($CH_2Cl_2$/AcOEt, 95:5) afforded compound **7** (159 mg, 84%) as a white solid. Mp 65 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 8.25–8.23 (m, 1H), 8.03–8.01 (m, 1H), 7.93–7.91 (m, 2H), 7.68–7.60 (m, 3H), 7.50–7.46 (m, 2H), 7.38 (d, $^3J_{HH}$ = 8.1 Hz, 1H), 6.03 (ddd, $^2J_{HF}$ = 47.4 Hz, $^3J_{HH}$ = 7.4 Hz, $^3J_{HH}$ = 4.5 Hz, 1H), 5.82 (d, $^3J_{HH}$ = 8.1 Hz, 1H), 4.75 (ddd, $^3J_{HF}$ = 22.8 Hz, $^2J_{HH}$ = 15.0 Hz, $^3J_{HH}$ = 4.5 Hz, 1H), 4.40 (ddd, $^3J_{HF}$ = 12.7 Hz, $^2J_{HH}$ = 15.0 Hz, $^3J_{HH}$ = 7.4 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.1, 161.9, 161.0, 152.6, 149.6, 144.4, 137.3, 135.3, 131.0, 130.4 (2C), 129.2 (2C), 128.8, 128.1, 125.8, 122.3, 102.9, 97.3 (d, $^1J_{CF}$ = 225.4 Hz), 46.5 (d, $^2J_{CF}$ = 22.7 Hz); $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –182.3 (ddd, $^2J_{FH}$ = 47.4 Hz, $^3J_{FH}$ = 22.8 Hz, $^3J_{FH}$ = 12.7 Hz, 1F); HRMS (ESI) *m/z* [M + Na]$^+$ calcd for $C_{20}H_{14}FN_3NaO_5S_2$ 482.0257, found 482.0245.

**General procedure B: conjugate addition of nucleic bases (purine series) onto fluorovinylsulfone.** To a solution of nucleic base (1.1 equiv) in DMF (0.2 M) were added TBAF (1 M in THF, 0.2 equiv) and 2-(1-fluoroethenesulfonyl)-1,3-benzothiazole **1** (1 equiv). The mixture was stirred for 24 h at 20 °C, quenched with a saturated aqueous solution of $NH_4Cl$ and extracted with $CH_2Cl_2$. Combined organic layers were dried over $MgSO_4$, filtered and evaporated under reduced pressure. The crude product was purified by filtration to give fluorinated aminosulfones **8**-**9**.

**9-[2-(1,3-Benzothiazole-2-sulfonyl)-2-fluoroethyl]-6-chloro-9H-purine (8).** General procedure B was followed with sulfone **1** (1.0 g, 4.11 mmol, 1 equiv), 6-chloropurine (703 mg, 4.52 mmol, 1.1 equiv) and TBAF (1 M in THF, 0.82 mL, 0.82 mmol, 0.2 equiv) in DMF (20 mL). The $CH_2Cl_2$ was added to the crude product and the pure solid compound **8** was recovered by filtration (1.21 g, 74%) as a yellow solid. Mp 207 °C; $^1$H NMR (DMSO, 400 MHz) $\delta$ 8.81 (s, 1H), 8.73 (s, 1H), 8.41–8.39 (m, 1H), 8.32–8.29 (m, 1H), 7.80–7.74 (m, 2H), 6.77 (ddd, $^2J_{HF}$ = 46.0 Hz, $^3J_{HH}$ = 7.5 Hz, $^3J_{HH}$ = 3.0 Hz, 1H), 5.34-5.10 (m, 2H); $^{13}$C NMR (DMSO, 100 MHz) $\delta$ 161.5, 152.2, 152.1, 151.9, 149.1, 147.5, 137.1, 130.5, 128.9, 128.4, 125.3, 123.7, 99.0 (d, $^1J_{CF}$ = 223.5 Hz), 41.2 (d, $^2J_{CF}$ = 20.2 Hz); $^{19}$F NMR (DMSO, 376 MHz) $\delta$ –181.9 (ddd, $^2J_{FH}$ = 46.0 Hz, $^3J_{FH}$ = 27.9 Hz, $^3J_{FH}$ = 19.2 Hz, 1F); MS (ESI) *m/z* 398 [M + H]$^+$ (100), 244 (79); HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{14}H_{10}ClFN_5O_2S_2$ 397.9948 and 399.9919, found 397.9953 and 399.9921.

***N*-{9-[2-(1,3-Benzothiazole-2-sulfonyl)-2-fluoroethyl]-6-oxo-6,9-dihydro-1H-purine-2-yl}-2-methylpropanamide (9).** General procedure B was followed with sulfone **1** (200 mg, 0.82 mmol, 1 equiv), $N^2$-(isobutanoyl)-guanine (200 mg, 0.90 mmol, 1.1 equiv) and TBAF (1 M in THF, 0.16 mL, 0.16 mmol, 0.2 equiv) in DMF (4 mL). The $CH_2Cl_2$ was added to the crude product and the pure solid compound **9** was recovered by filtration (279 mg, 73%) as a beige solid as a mixture of regioisomers ($N^9/N^7$, 3:2). Mp 153 °C; $^1$H NMR (DMSO, 400 MHz) $\delta$ 12.18 (s, 1H, $N^9$-isomer), 12.10 (s, 1H, $N^7$-isomer), 11.75 (s, 1H, $N^7$-isomer), 11.58 (s, 1H, $N^9$-isomer), 8.41–8.39 (m, 2H, $N^9$ and $N^7$-isomer), 8.35–8.32 (m, 2H, $N^9$ and $N^7$-isomer), 8.25 (s, 1H, $N^9$-isomer), 8.05 (s, 1H, $N^7$-isomer), 7.79–7.76 (m, 4H, $N^9$ and $N^7$-isomer), 6.69 (ddd, $^2J_{HF}$ = 46.6 Hz, $^3J_{HH}$ = 8.4 Hz, $^3J_{HH}$ = 3.0 Hz, 1H, $N^7$-isomer), 6.65 (ddd, $^2J_{HF}$ = 46.6 Hz, $^3J_{HH}$ = 8.4 Hz, $^3J_{HH}$ = 3.0 Hz, 1H, $N^9$-isomer), 5.32–4.84 (m, 4H, $N^9$ and $N^7$-isomers), 2.81-2.69 (m, 2H, $N^9$ and $N^7$-isomers), 1.13–1.10 (m, 12H, $N^9$ and $N^7$-isomer); $^{13}$C NMR (DMSO, 100 MHz) $\delta$ 180.3 ($N^7$-isomer), 180.0 ($N^9$-isomer), 161.5 (2C, $N^9$ and $N^7$-isomers), 157.2 ($N^9$-isomer), 154.7 ($N^7$-isomer), 152.7 ($N^9$-isomer), 152.3 (2C, ($N^9$ and $N^7$-isomer)), 149.0 ($N^7$-isomer), 148.2 ($N^7$-isomer), 147.4 ($N^9$-isomer), 145.2 ($N^9$-isomer), 140.0 ($N^9$-isomer), 137.2 (2C, $N^9$ and $N^7$-isomer), 128.9 (2C, $N^9$ and $N^7$-isomer), 128.4 (2C, $N^9$ and $N^7$-isomer), 125.4 (2C, $N^9$ and $N^7$-isomer), 123.7 (2C, $N^9$ and $N^7$-isomer), 119.8 ($N^7$-isomer), 111.4 ($N^9$-isomer), 99.4 (d, $^1J_{CF}$ = 222.9 Hz, $N^9$-isomer), 99.0 (d, $^1J_{CF}$ = 223.5 Hz, $N^7$-isomer), 43.7 (d, $^2J_{CF}$ = 20.9 Hz, $N^9$-isomer), 40.5 (d, $^2J_{CF}$ = 20.7 Hz, $N^7$-isomer), 18.9 (4C, $N^9$ and $N^7$-isomer), 13.5 (2C, $N^9$ and $N^7$-isomer); $^{19}$F NMR (DMSO, 376 MHz) $\delta$ –182.4 (ddd, $^2J_{FH}$ = 46.6 Hz, $^3J_{FH}$ = 30.7 Hz, $^3J_{FH}$ = 16.0 Hz, 1F, $N^7$-isomer), –184.0 (ddd, $^2J_{FH}$ = 46.6 Hz, $^3J_{FH}$ = 29.5 Hz, $^3J_{FH}$ = 15.1 Hz, 1F, $N^9$-isomer); MS (ESI) *m/z* 465 $[M + H]^+$ (42), 395 (35), 244 (100), 222 (18); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{18}H_{18}FN_6O_4S_2$ 465.0815, found 465.0824.

**3-Benzoyl-1-[2-(1,3-benzothiazole-2-sulfonyl)-2-fluoroethyl]-5-fluoro-1,2,3,4-tetrahydropyrimidine-2,4-dione (10).** To a solution of sulfone **5** (400 mg, 1.071 mmol, 1 equiv) and pyridine (0.26 mL, 3.21 mmol, 3 equiv) in MeCN (1 mL) were added dropwise benzoyl chloride (0.14 mL, 1.18 mmol, 1.1 equiv) at 0 °C. The mixture was stirred for 48 h at 20 °C then toluene was added. The solvents were removed by evaporation under reduced pressure. The crude product was purified by flash chromatography ($CH_2Cl_2$/AcOEt, 96:4) to give the sulfone **10** (473 mg, 93%) as a white solid. Mp 135 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 8.30–8.27 (m, 1H), 8.08–8.06 (m, 1H), 7.95–7.93 (m, 2H), 7.73–7.65 (m, 3H), 7.55–7.50 (m, 3H), 6.03 (ddd, $^2J_{HF}$ = 47.3 Hz, $^3J_{HH}$ = 7.0 Hz, $^3J_{HH}$ = 5.0 Hz, 1H), 4.75 (ddd, $^3J_{HF}$ = 20.5 Hz, $^2J_{HH}$ = 15.2 Hz, $^3J_{HH}$ = 5.0 Hz, 1H), 4.42 (ddd, $^3J_{HF}$ = 12.6 Hz, $^2J_{HH}$ = 15.2 Hz, $^3J_{HH}$ = 7.0 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 166.8, 168.8, 156.0 (d, $^2J_{CF}$ = 25.8 Hz), 152.5, 148.2,

140.2 (d, $^{1}J_{CF}$ = 239.5 Hz), 137.3, 135.6, 130.5 (2C), 130.4, 129.3 (2C), 128.9 (d, $^{2}J_{CF}$ = 32.8 Hz), 128.8, 128.1, 125.7, 122.3, 97.4 (d, $^{1}J_{CF}$ = 225.3 Hz), 46.3 (d, $^{2}J_{CF}$ = 22.8 Hz); $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –162.8 (d, $^{3}J_{FH}$ = 5.3 Hz, 1F), –182.3 (ddd, $^{2}J_{FH}$ = 47.3 Hz, $^{3}J_{FH}$ = 20.5 Hz, $^{3}J_{FH}$ = 12.6 Hz, 1F); MS (ESI) *m/z* 478 $[M + H]^+$ (100), 105 (55); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{20}H_{14}F_2N_3O_5S_2$ 478.0343, found 478.0349.

**General procedure C: preparation of fluorinated allylamines in the presence of NaHMDS.** To a solution of fluoroaminosulfone **5-10** (1 equiv), and aldehyde (1.05 equiv) at –78 °C in THF (0.1 M) was added NaHMDS (1 M in THF, 1.5 equiv). After 30 min at –78 °C, the mixture was stirred for 1 h 30 at –20 °C, quenched with a saturated aqueous solution of $NH_4Cl$ and extracted with $CH_2Cl_2$. Combined organic layers were washed with brine, dried over $MgSO_4$, filtered and evaporated under reduced pressure. The crude product was purified by flash column chromatography to give amino-alkenes **11-30a**.

**(*Z*/*E*)-3-Benzoyl-1-(2-fluoro-3-phenylprop-2-en-1-yl)-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (11).** General procedure C was followed with aminosulfone **6** (100 mg, 0.21 mmol, 1 equiv), benzaldehyde (23 μL, 0.22 mmol, 1.05 equiv) and NaHMDS (1 M in THF, 0.32 mL, 0.32 mmol, 1.5 equiv) in THF (2 mL). The purification by flash chromatography (pentane/AcOEt, 6:4) afforded compound **11** (67 mg, 87%) as a white oil (*E*/*Z* = 5:95). (*Z*)-**11**: $^{1}$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.94–7.92 (m, 2H), 7.66–7.62 (m, 1H), 7.51–7.46 (m, 4H), 7.38–7.34 (m, 2H), 7.31–7.27 (m, 1H), 7.23 (t, $^{4}J_{HH}$ = 1.0 Hz, 1H), 5.88 (d, $^{3}J_{HF\textit{trans}}$ = 38.1 Hz, 1H), 4.55 (d, $^{3}J_{HF}$ = 18.0 Hz, 2H), 1.96 (d, $^{4}J_{HH}$ = 1.0 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.8, 162.9, 152.5 (d, $^{1}J_{CF}$ = 266.6 Hz), 149.6, 139.1, 135.0, 131.7 (d, $^{3}J_{CF}$ = 3.5 Hz), 131.4, 130.3 (2C), 129.1 (2C), 128.9 (d, $^{4}J_{CF}$ = 7.3 Hz, 2C), 128.6 (2C), 128.2 (d, $^{6}J_{CF}$ = 2.5 Hz), 111.5 (d, $^{2}J_{CF}$ = 6.4 Hz), 111.2, 48.9 (d, $^{2}J_{CF}$ = 29.1 Hz), 12.3; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –111.2 (dt, $^{3}J_{FH\textit{trans}}$ = 38.1 Hz, $^{3}J_{FH}$ = 18.0 Hz, 1F); MS (EI) *m/z* 364 $[M]^{+\bullet}$ (44), 105 (100), 77 (34); HRMS (ESI) *m/z* $[M + Na]^+$ calcd for $C_{21}H_{17}FN_2NaO_3$ 387.1121, found 387.1139. (*E*)-**11**: $^{1}$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.93–7.91 (m, 2H), 7.66–7.63 (m, 1H), 7.51–7.47 (m, 2H), 7.39–7.35 (m, 2H), 7.32–7.28 (m, 3H), 7.06 (m, 1H), 6.61 (d, $^{3}J_{HF\textit{cis}}$ = 20.5 Hz, 1H), 4.74 (d, $^{3}J_{HF}$ = 17.2 Hz, 2H), 1.95 (d, $^{4}J_{HH}$ = 1.0 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.7, 162.9, 153.5 (d, $^{1}J_{CF}$ = 254.2 Hz), 149.7, 139.0, 135.0, 131.5 (d, $^{3}J_{CF}$ = 11.4 Hz), 131.4, 130.5 (2C), 129.1 (2C), 128.9 (2C), 128.6 (d, $^{4}J_{CF}$ = 2.7 Hz, 2C), 128.1, 113.9 (d, $^{2}J_{CF}$ = 24.6 Hz), 111.3, 44.7 (d, $^{2}J_{CF}$ = 26.9 Hz), 12.5; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –109.2 (dt, $^{3}J_{FH\textit{cis}}$ = 20.4 Hz, $^{3}J_{FH}$ = 17.9 Hz, 1F); MS (EI) *m/z* 364

$[M]^{+\bullet}$ (44), 105 (100), 77 (34); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{21}H_{17}FN_2NaO_3$ 387.1121, found 387.1139.

**(*Z*/*E*)-3-Benzoyl-1-(2-fluoro-3-phenylprop-2-en-1-yl)-1,2,3,4-tetrahydropyrimidine-2,4-dione (12).** General procedure C was followed with aminosulfone **7** (100 mg, 0.22 mmol, 1 equiv), benzaldehyde (23 μL, 0.23 mmol, 1.05 equiv) and NaHMDS (1 M in THF, 0.33 mL, 0.33 mmol, 1.5 equiv) in THF (2.2 mL). The purification by flash chromatography (pentane/AcOEt, 1:1) afforded compound **12** (53 mg, 69%) as a yellow oil (*E*/*Z* = 6:94). (*Z*)-**12**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.96–7.94 (m, 2H), 7.67–7.63 (m, 1H), 7.51–7.47 (m, 4H), 7.40 (d, $^3J_{HH}$ = 7.9 Hz, 1H), 7.38–7.28 (m, 3H), 5.89 (d, $^3J_{HF\textit{trans}}$ = 38.3 Hz, 1H), 5.84 (d, $^3J_{HH}$ = 7.9 Hz, 1H), 4.57 (d, $^3J_{HF}$ = 17.9 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.5, 162.1, 152.1 (d, $^1J_{CF}$ = 266.5 Hz), 149.6, 143.3, 135.2, 131.6 (d, $^3J_{CF}$ = 3.2 Hz), 131.2, 130.4 (2C), 129.2 (2C), 129.0 (d, $^4J_{CF}$ = 7.1 Hz, 2C), 128.6 (2C), 128.3 (d, $^6J_{CF}$ = 2.1 Hz), 111.9 (d, $^2J_{CF}$ = 5.8 Hz), 102.6, 49.3 (d, $^2J_{CF}$ = 29.0 Hz); $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –111.6 (dt, $^3J_{FH\textit{trans}}$ = 38.3 Hz, $^3J_{FH}$ = 17.9 Hz, 1F); MS (ESI) *m/z* 351 $[M + H]^+$ (52), 135 (26), 105 (100); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{20}H_{16}FN_2O_3$ 351.1145, found 351.1148. (*E*)-**12**: $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –109.2 (dt, $^3J_{FH\textit{cis}}$ = 20.4 Hz, $^3J_{FH}$ = 17.9 Hz, 1F); MS (ESI) *m/z* 351 $[M + H]^+$ (52), 135 (26), 105 (100); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{20}H_{16}FN_2O_3$ 351.1145, found 351.1148.

**(*Z*/*E*)-5-Fluoro-1-(2-fluoro-3-phenylprop-2-en-1-yl)-1,2,3,4-tetrahydropyrimidine-2,4-dione (13).** General procedure C was followed with aminosulfone **5** (100 mg, 0.27 mmol, 1 equiv), benzaldehyde (29 μL, 0.28 mmol, 1.05 equiv) and NaHMDS (1 M in THF, 0.80 mL, 0.80 mmol, 3 equiv) in THF (3 mL). The purification by flash chromatography ($CH_2Cl_2$/AcOEt, 85:15) afforded compound **13** (49 mg, 69%) as a colorless oil (*E*/*Z* = 47:53). $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 9.10 (s, 2H, *E* and *Z*), 7.51–7.21 (m, 12H, *E* and *Z*), 6.62 (d, $^3J_{HF\textit{cis}}$ = 20.3 Hz, 1H, *E*), 5.92 (d, $^3J_{HF\textit{trans}}$ = 38.1 Hz, 1H, *Z*), 4.70 (d, $^3J_{HF}$ = 17.8 Hz, 2H, *E*), 4.55 (d, $^3J_{HF}$ = 17.6 Hz, 2H, *Z*); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 156.7 (d, $^2J_{CF}$ = 27.3 Hz, *E*), 156.7 (d, $^2J_{CF}$ = 26.5 Hz, *Z*), 153.2 (d, $^1J_{CF}$ = 253.5 Hz, *Z*), 151.9 (d, $^1J_{CF}$ = 266.3 Hz, *E*), 149.2 (*Z*), 149.1 (*E*), 140.8 (d, $^1J_{CF}$ = 239.8 Hz, *E*), 140.6 (d, $^1J_{CF}$ = 238.9 Hz, *Z*), 131.4 (d, $^3J_{CF}$ = 3.5 Hz, *E*), 131.3 (d, $^3J_{CF}$ = 11.5 Hz, *Z*), 129.1 (*Z* or *E*), 129.0 (2C, *Z* or *E*), 128.8 (*Z* or *E*), 128.7 (*Z* or *E*), 128.6 (d, $^4J_{CF}$ = 2.5 Hz, 2C, *Z*), 128.4 (d, $^4J_{CF}$ = 2.0 Hz, 2C, *E*), 128.3 (*Z* or *E*), 127.6 (d, $^2J_{CF}$ = 33.2 Hz, *E*), 127.5 (d, $^2J_{CF}$ = 32.2 Hz, *Z*), 114.4 (d, $^2J_{CF}$ = 23.8 Hz, *Z*), 112.1 (d, $^2J_{CF}$ = 6.4 Hz, *E*), 49.3 (d, $^2J_{CF}$ = 29.7 Hz, *E*), 44.9 (d, $^2J_{CF}$ = 27.7 Hz, *Z*); $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –109.1 (dt, $^3J_{FH\textit{cis}}$ = 20.3 Hz, $^3J_{FH}$ = 17.8 Hz, 1F, *E*), –111.4 (dt, $^3J_{FH\textit{trans}}$ = 38.1 Hz,

$^3J_{FH}$ = 17.6 Hz, *Z*), –164.4 (m, 1F, *E* and *Z*); MS (ESI) *m/z* 365 $[M + H]^+$ (34), 135 (100); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{13}H_{11}F_2N_2O_2$ 265.0789, found 265.0796.

**(*Z*/*E*)-3-Benzoyl-5-fluoro-1-(2-fluoro-3-phenylprop-2-en-1-yl)-1,2,3,4-tetrahydropyrimidine-2,4-dione (14).** General procedure C was followed with aminosulfone **10** (130 mg, 0.27 mmol, 1 equiv), benzaldehyde (29 µL, 0.29 mmol, 1.05 equiv) and NaHMDS (1 M in THF, 0.41 mL, 0.41 mmol, 1.5 equiv) in THF (3 mL). The purification by flash chromatography (pentane/AcOEt, 6:4) afforded compound **14** (39 mg, 39%) as a yellow oil (*E*/*Z* = 5:95). (*Z*)-**14**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.94–7.92 (m, 2H), 7.69–7.65 (m, 1H), 7.52–7.48 (m, 5H), 7.38–7.29 (m, 3H), 5.90 (d, $^3J_{HFtrans}$ = 38.2 Hz, 1H), 4.55 (d, $^3J_{HF}$ = 17.8 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 167.0, 156.1 (d, $^2J_{CF}$ = 26.0 Hz), 151.7 (d, $^1J_{CF}$ = 265.7 Hz), 148.2, 140.1 (d, $^1J_{CF}$ = 239.7 Hz), 135.5, 131.4 (d, $^3J_{CF}$ = 2.9 Hz), 130.8, 130.5 (2C), 129.3 (2C), 129.0 (d, $^4J_{CF}$ = 7.3 Hz, 2C), 128.6 (2C), 128.4 (d, $^6J_{CF}$ = 2.2 Hz), 127.5 (d, $^2J_{CF}$ = 32.5 Hz), 112.4 (d, $^2J_{CF}$ = 6.5 Hz), 49.5 (d, $^2J_{CF}$ = 28.9 Hz); $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –111.8 (dt, $^3J_{FHtrans}$ = 38.2 Hz, $^3J_{FH}$ = 17.8 Hz, 1F), –163.7 (d, $^3J_{FH}$ = 5.2 Hz, 1F); MS (ESI) *m/z* 369 $[M + H]^+$ (100), 135 (69), 105 (78); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{20}H_{15}F_2N_2O_3$ 369.1051, found 369.1063. (*E*)-**14**: $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –109.2 (dt, $^3J_{FHcis}$ = 20.1 Hz, $^3J_{FH}$ = 17.4 Hz, 1F), –163.5 (d, $^3J_{FH}$ = 5.2 Hz, 1F); MS (ESI) *m/z* 369 $[M + H]^+$ (100), 135 (69), 105 (78); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{20}H_{15}F_2N_2O_3$ 369.1051, found 369.1063.

**General procedure D: preparation of fluorinated allylamines in the presence of *t*BuOK.** To a solution of fluoroaminosulfone **8-9** (1 equiv), and aldehyde (1.05 equiv) at –17 °C in THF (0.1 M) was added *t*BuOK (2 equiv). After 10 min at –17 °C, the mixture was stirred at 20 °C, (4 h to 8 h) quenched with a saturated aqueous solution of $NH_4Cl$ and extracted with $CH_2Cl_2$. Combined organic layers were washed with brine, dried over $MgSO_4$, filtered and evaporated under reduced pressure. The crude product was purified by flash column chromatography to give amino-alkenes **15-16**.

**(*Z*/*E*)-6-Chloro-9-(2-fluoro-3-phenylprop-2-en-1-yl)-9H-purine (15).** General procedure D was followed with aminosulfone **8** (100 mg, 0.25 mmol, 1 equiv), benzaldehyde (27 µL, 0.26 mmol, 1.05 equiv) and *t*BuOK (37 mg, 0.33 mmol, 2 equiv) in THF (2.5 mL). The mixture was stirred during 4 h. The purification by flash chromatography ($CH_2Cl_2$/AcOEt, 9:1) afforded compound **15** (47 mg, 61%) as a colorless oil (*E*/*Z* = 55:45). (*Z*)-**15**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 8.78 (s, 1H), 8.26 (s, 1H), 7.50–7.47 (m, 2H), 7.36–7.28 (m, 3H), 5.99 (d, $^3J_{HFtrans}$ = 37.7 Hz, 1H), 5.12 (d, $^3J_{HF}$ = 17.1 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 152.3, 151.7, 151.6 (d, $^1J_{CF}$ = 265.8 Hz), 151.3, 144.7, 131.5, 131.3 (d, $^3J_{CF}$ = 3.4 Hz), 128.8 (d, $^4J_{CF}$

= 7.3 Hz, 2C), 128.7 (2C), 128.4 (d, $^{6}J_{CF}$ = 2.4 Hz), 111.4 (d, $^{2}J_{CF}$ = 6.3 Hz), 45.5 (d, $^{2}J_{CF}$ = 30.7 Hz); $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –110.6 (dt, $^{3}J_{FHtrans}$ = 37.7 Hz, $^{3}J_{FH}$ = 17.1 Hz, 1F); MS (ESI) *m/z* 289 [M + H]$^+$ (100), 135 (21); HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{14}H_{11}ClFN_4$ 289.0656 and 291.0627, found 289.0669 and 291.0636. (*E*)-**15**: $^{1}$H NMR ($CDCl_3$, 400 MHz) $\delta$ 8.77 (s, 1H), 8.17 (d, $^{5}J_{HF}$ = 1.1 Hz, 1H), 7.44–7.33 (m, 5H), 6.64 (d, $^{3}J_{HFcis}$ = 19.6 Hz, 1H), 5.22 (d, $^{3}J_{HF}$ = 19.1 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 152.9 (d, $^{1}J_{CF}$ = 254.1 Hz), 152.2, 151.7, 151.2, 144.8 (d, $^{5}J_{CF}$ = 1.6 Hz), 131.5 (d, $^{3}J_{CF}$ = 11.5 Hz), 131.3, 129.0 (2C), 128.6 (d, $^{4}J_{CF}$ = 2.4 Hz, 2C), 128.3, 114.0 (d, $^{2}J_{CF}$ = 24.1 Hz), 41.5 (d, $^{2}J_{CF}$ = 28.3 Hz); $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –107.2 (dt, $^{3}J_{FHcis}$ = 19.6 Hz, $^{3}J_{FH}$ = 19.1 Hz, 1F); MS (ESI) *m/z* 289 [M + H]$^+$ (100), 135 (21); HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{14}H_{11}ClFN_4$ 289.0656 and 291.0627, found 289.0669 and 291.0636.

**(*Z*/*E*)-*N*-[9-(2-Fluoro-3-phenylprop-2-en-1-yl)-6-oxo-6,9-dihydro-1H-purin-2-yl]-2-methylpropanamide (16).** General procedure D was followed with aminosulfone **9** (100 mg, 0.22 mmol, 1 equiv), benzaldehyde (23 μL, 0.23 mmol, 1.05 equiv) and *t*BuOK (48 mg, 0.43 mmol, 2 equiv) in THF (2.1 mL). The mixture was stirred during 8 h. The purification by flash chromatography ($CH_2Cl_2$/MeOH, 94:6) afforded compound **16** (42 mg, 55%) as a white oil (*E*/*Z* = 2:3). $N^7$-(*Z*)-**16**: $^{1}$H NMR ($CDCl_3$, 400 MHz) $\delta$ 12.02 (s, 1H), 8.26 (s, 1H), 7.77 (s, 1H), 7.47–7.44 (m, 2H), 7.35–7.27 (m, 3H), 5.74 (d, $^{3}J_{HFtrans}$ = 37.9 Hz, 1H), 4.84 (d, $^{3}J_{HF}$ = 15.2 Hz, 2H), 2.68-2.62 (m, 1H), 1.30 (s, 3H), 1.28 (s, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 178.0, 155.5, 152.7 (d, $^{1}J_{CF}$ = 288.9 Hz), 151.3, 147.5, 138.6, 131.6 (d, $^{3}J_{CF}$ = 3.4 Hz), 128.8 (d, $^{4}J_{CF}$ = 7.4 Hz, 2C), 128.7 (2C), 128.3 (d, $^{6}J_{CF}$ = 2.9 Hz), 121.2, 110.1 (d, $^{2}J_{CF}$ = 6.9 Hz), 44.7 (d, $^{2}J_{CF}$ = 32.4 Hz), 36.6, 19.0 (2C); $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –110.0 (dt, $^{3}J_{FHtrans}$ = 37.9 Hz, $^{3}J_{FH}$ = 15.2 Hz, 1F); MS (ESI) *m/z* 356 [M + H]$^+$ (52), 222 (13), 135 (100); HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{18}H_{19}FN_5O_2$ 356.1523, found 356.1526. $N^9$-(*Z*)-**16**, $N^9$-(*E*)-**16** & $N^7$-(*E*)-**16**: $^{1}$H NMR ($CDCl_3$, 400 MHz) $\delta$ 12.59, 12.38, 12.35 (s, 3H, $Z^{N9}$, $E^{N9}$ and $E^{N7}$), 10.73, 10.71, 9.84 (s, 3H, $Z^{N9}$, $E^{N9}$ and $E^{N7}$), 7.91 (s, 1H, $E^{N9}$), 7.83 (d, *J* = 1.0 Hz, 1H, $E^{N7}$), 7.72 (d, $^{5}J_{HF}$ = 0.8 Hz, 1H, $Z^{N9}$), 7.48-7.22 (m, 15H, $Z^{N9}$, $E^{N9}$, $E^{N7}$), 6.62 (d, $^{3}J_{HFcis}$ = 19.8 Hz, 1H, $E^{N7}$), 6.52 (d, $^{3}J_{HFcis}$ = 19.8 Hz, 1H, $E^{N9}$), 6.06 (d, $^{3}J_{HFtrans}$ = 37.9 Hz, 1H, $Z^{N9}$), 5.40 (d, $^{3}J_{HF}$ = 18.5 Hz, 2H, $E^{N7}$), 5.22 (d, $^{3}J_{HF}$ = 18.5 Hz, 2H, $E^{N9}$), 4.96 (d, $^{3}J_{HF}$ = 19.4 Hz, 2H, $Z^{N9}$), 2.96–2.83 (m, 3H, $Z^{N9}$, $E^{N9}$ and $E^{N7}$), 1.26–1.22 (m, 18H, $Z^{N9}$, $E^{N9}$ and $E^{N7}$); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 180.1 ($E^{N9}$), 180.0 ($E^{N7}$), 178.1 ($Z^{N9}$), 156.8 ($Z^{N9}$ or $E^{N9}$ or $E^{N7}$), 156.6 ($Z^{N9}$ or $E^{N9}$ or $E^{N7}$), 156.3 ($Z^{N9}$ or $E^{N9}$ or $E^{N7}$), 153.6 (d, $^{1}J_{CF}$ = 253.0 Hz, $E^{N9}$), 153.4 (d, $^{1}J_{CF}$ = 253.0 Hz, $E^{N7}$), 152.4 (d, $^{1}J_{CF}$ = 265.7 Hz, $Z^{N9}$), 153.1 ($Z^{N9}$ or $E^{N9}$ or $E^{N7}$), 149.0 ($Z^{N9}$ or $E^{N9}$ or $E^{N7}$), 148.3 ($Z^{N9}$ or $E^{N9}$ or $E^{N7}$), 148.2 ($Z^{N9}$ or $E^{N9}$ or $E^{N7}$), 147.3 ($Z^{N9}$ or $E^{N9}$ or $E^{N7}$), 143.0

($E^{N9}$), 142.5 ($E^{N7}$), 138.7 ($Z^{N9}$), 131.8 ($Z^{N9}$ or $E^{N9}$ or $E^{N7}$), 131.6 ($Z^{N9}$ or $E^{N9}$ or $E^{N7}$), 128.9 ($Z^{N9}$ or $E^{N9}$ or $E^{N7}$), 128.9 (2C, $Z^{N9}$ or $E^{N9}$ or $E^{N7}$), 128.8 (2C, $Z^{N9}$ or $E^{N9}$ or $E^{N7}$), 128.8 (2C, $Z^{N9}$ or $E^{N9}$ or $E^{N7}$), 128.5 (2C, $Z^{N9}$ or $E^{N9}$ or $E^{N7}$), 128.5 (2C, $Z^{N9}$ or $E^{N9}$ or $E^{N7}$), 128.5 (2C, $Z^{N9}$ or $E^{N9}$ or $E^{N7}$), 128.4 ($Z^{N9}$ or $E^{N9}$ or $E^{N7}$), 128.4 ($Z^{N9}$ or $E^{N9}$ or $E^{N7}$), 128.1 ($Z^{N9}$ or $E^{N9}$ or $E^{N7}$), 127.9 ($Z^{N9}$ or $E^{N9}$ or $E^{N7}$), 120.4 ($Z^{N9}$ or $E^{N9}$ or $E^{N7}$), 113.9 (d, $^2J_{CF}$ = 24.2 Hz, $E^{N9}$), 113.3 (d, $^2J_{CF}$ = 24.2 Hz, $E^{N7}$), 112.0 ($Z^{N9}$ or $E^{N9}$ or $E^{N7}$), 111.7 ($Z^{N9}$ or $E^{N9}$ or $E^{N7}$), 111.1 (d, $^2J_{CF}$ = 5.5 Hz, $Z^{N9}$), 48.2 (d, $^2J_{CF}$ = 29.1 Hz, $E^{N9}$), 44.0 (d, $^2J_{CF}$ = 27.7 Hz, $E^{N7}$), 40.9 (d, $^2J_{CF}$ = 29.1 Hz, $Z^{N9}$), 38.7 ($E^{N7}$), 35.9 ($E^{N9}$), 35.9 ($Z^{N9}$), 19.0 (6C, $Z^{N9}$, $E^{N9}$ and $E^{N7}$); $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –106.6 (dt, $^3J_{FHcis}$ = 19.8 Hz, $^3J_{FH}$ = 18.5 Hz, 1F, $E^{N9}$), –107.4 (dt, $^3J_{FHcis}$ = 19.8 Hz, $^3J_{FH}$ = 18.5 Hz, 1F, $E^{N7}$), –111.1 (dt, $^3J_{FHtrans}$ = 37.9 Hz, $^3J_{FH}$ = 19.4 Hz, 1F, $Z^{N9}$); MS (ESI) *m/z* 356 [M + H]$^+$ (52), 222 (13), 135 (100); HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{18}H_{19}FN_5O_2$ 356.1523, found 356.1526.

**(*Z*/*E*)-3-Benzoyl-1-[2-fluoro-3-(4-methoxyphenyl)prop-2-en-1-yl]-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (17a).** General procedure C was followed with aminosulfone **6** (100 mg, 0.21 mmol, 1 equiv), *p*-methoxybenzaldehyde (27 μL, 0.22 mmol, 1.05 equiv) and NaHMDS (1 M in THF, 0.32 mL, 0.32 mmol, 1.5 equiv) in THF (2 mL). The purification by flash chromatography (pentane/AcOEt, 6:4) afforded compound **17a** (66 mg, 79%) as a colorless oil (*E*/*Z* = 4:96). (*Z*)-**17a**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.93–7.91 (m, 2H), 7.65–7.61 (m, 1H), 7.50–7.43 (m, 4H), 7.23 (s, 1H), 6.89–6.87 (m, 2H), 5.82 (d, $^3J_{HFtrans}$ = 38.6 Hz, 1H), 4.53 (d, $^3J_{HF}$ = 18.4 Hz, 2H), 3.81 (s, 3H), 1.96 (s, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.8, 162.9, 159.3 (d, $^6J_{CF}$ = 2.8 Hz), 151.1 (d, $^1J_{CF}$ = 163.4 Hz), 149.6, 139.1, 135.0, 131.4, 130.3 (2C), 130.2 (d, $^4J_{CF}$ = 7.9 Hz, 2C), 129.1 (2C), 124.3 (d, $^3J_{CF}$ = 3.0 Hz), 113.9 (2C), 111.2 (d, $^2J_{CF}$ = 8.5 Hz), 111.1, 55.2, 48.9 (d, $^2J_{CF}$ = 29.3 Hz), 12.3; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –114.2 (dt, $^3J_{FHtrans}$ = 38.6 Hz, $^3J_{FH}$ = 18.4 Hz, 1F); MS (EI) *m/z* 395 [M + H]$^+$ (81), 165 (100); HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{22}H_{20}FN_2O_4$ 395.1407, found 395.1408. (*E*)-**17a**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.93–7.91 (m, 2H), 7.66–7.63 (m, 1H), 7.51–7.47 (m, 2H), 7.23–7.21 (m, 2H), 7.08 (m, 1H), 6.90–6.88 (m, 2H), 6.54 (d, $^3J_{HFcis}$ = 20.7 Hz, 1H), 4.73 (d, $^3J_{HF}$ = 17.6 Hz, 2H), 3.80 (s, 3H), 1.95 (d, $^4J_{HH}$ = 0.9 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.7, 162.9, 159.4, 152.7 (d, $^1J_{CF}$ = 250.0 Hz), 149.8, 139.0, 135.0, 131.5, 130.5 (2C), 129.8 (d, $^4J_{CF}$ = 2.5 Hz, 2C), 129.1 (2C), 123.7 (d, $^3J_{CF}$ = 11.8 Hz), 114.4 (2C), 113.6 (d, $^2J_{CF}$ = 25.3 Hz), 111.2, 55.3, 44.8 (d, $^2J_{CF}$ = 27.7 Hz), 12.5; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –110.2 (dt, $^3J_{FHcis}$ = 20.7 Hz, $^3J_{FH}$ = 17.6 Hz, 1F); MS (EI) *m/z* 395 [M + H]$^+$ (81), 165 (100); HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{22}H_{20}FN_2O_4$ 395.1407, found 395.1408.

**(*Z*/*E*)-3-Benzoyl-1-[3-(4-bromophenyl)-2-fluoroprop-2-en-1-yl]-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (18a).** General procedure C was followed with aminosulfone **6** (100 mg, 0.21 mmol, 1 equiv), *p*-bromobenzaldehyde (41 mg, 0.22 mmol, 1.05 equiv) and NaHMDS (1 M in THF, 0.32 mL, 0.32 mmol, 1.5 equiv) in THF (2 mL). The purification by flash chromatography (pentane/AcOEt, 6:4) afforded compound **18a** (81 mg, 86%) as a yellow solid (*E*/*Z* = 8:92). Mp 219 °C; (*Z*)-**18a**: $^{1}$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.93–7.91 (m, 2H), 7.66–7.62 (m, 1H), 7.51–7.46 (m, 4H), 7.38–7.34 (m, 2H), 7.20 (t, $^{4}J_{HH}$ = 1.0 Hz, 1H), 5.83 (d, $^{3}J_{HF\textit{trans}}$ = 37.6 Hz, 1H), 4.55 (d, $^{3}J_{HF}$ = 17.9 Hz, 2H), 1.99 (d, $^{4}J_{HH}$ = 1.0 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.7, 162.9, 153.0 (d, $^{1}J_{CF}$ = 267.6 Hz), 149.6, 139.1, 135.1, 131.7 (2C), 131.4, 130.6 (d, $^{6}J_{CF}$ = 2.8 Hz), 130.5, 130.4 (3C), 129.1 (2C), 122.1 (d, $^{2}J_{CF}$ = 3.6 Hz), 111.4, 110.5 (d, $^{2}J_{CF}$ = 6.1 Hz), 49.0 (d, $^{2}J_{CF}$ = 29.4 Hz), 12.4; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –110.0 (dt, $^{3}J_{FH\textit{trans}}$ = 37.6 Hz, $^{3}J_{FH}$ = 17.9 Hz, 1F); MS (EI) *m/z* 444 $[M]^{+\bullet}$ (22), 442 (21), 105 (100), 77 (32); HRMS (ESI) *m/z* $[M + Na]^+$ calcd for $C_{21}H_{16}BrFN_2NaO_3$ 465.0226, found 465.0210. (*E*)-**18a**: $^{1}$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.92–7.90 (m, 2H), 7.66–7.62 (m, 1H), 7.51–7.46 (m, 4H), 7.20–7.18 (m, 2H), 7.07 (t, $^{4}J_{HH}$ = 1.1 Hz, 1H), 6.49 (d, $^{3}J_{HF\textit{cis}}$ = 20.3 Hz, 1H), 4.68 (d, $^{3}J_{HF}$ = 17.4 Hz, 2H), 1.95 (d, $^{4}J_{HH}$ = 1.1 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.6, 162.9, 153.9 (d, $^{1}J_{CF}$ = 254.3 Hz), 149.7, 139.2, 135.1, 132.0 (2C), 131.4, 130.5 (2C), 130.4, 130.2 (d, $^{4}J_{CF}$ = 2.7 Hz, 2C), 129.1 (2C), 122.2, 112.7 (d, $^{2}J_{CF}$ = 25.7 Hz), 111.4, 45.0 (d, $^{2}J_{CF}$ = 26.4 Hz), 12.5; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –107.6 (dt, $^{3}J_{FH\textit{cis}}$ = 20.3 Hz, $^{3}J_{FH}$ = 17.4 Hz, 1F); MS (EI) *m/z* 444 $[M]^{+\bullet}$ (22), 442 (21), 105 (100), 77 (32); HRMS (ESI) *m/z* $[M + Na]^+$ calcd for $C_{21}H_{16}BrFN_2NaO_3$ 465.0226, found 465.0210.

**(*Z*/*E*)-3-Benzoyl-1-[2-fluoro-3-(4-nitrophenyl)prop-2-en-1-yl]-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (19a).** General procedure C was followed with aminosulfone **6** (100 mg, 0.21 mmol, 1 equiv), *p*-nitrobenzaldehyde (34 mg, 0.22 mmol, 1.05 equiv) and NaHMDS (1 M in THF, 0.32 mL, 0.32 mmol, 1.5 equiv) in THF (2 mL). The purification by flash chromatography (pentane/AcOEt, 1:1) afforded compound **19a** (54 mg, 63%) as a yellow oil (*E*/*Z* = 32:68). (*Z*)-**19a**: $^{1}$H NMR ($CDCl_3$, 400 MHz) $\delta$ 8.18 (d, $^{3}J_{HH}$ = 9.0 Hz, 2H), 7.93–7.91 (m, 2H), 7.67–762 (m, 3H), 7.50–7.46 (m, 2H), 7.22 (m, 1H), 5.97 (d, $^{3}J_{HF\textit{trans}}$ = 36.7 Hz, 1H), 4.60 (d, $^{3}J_{HF}$ = 17.4 Hz, 2H), 1.98 (d, $^{4}J_{HH}$ = 0.7 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.6, 162.8, 155.3 (d, $^{1}J_{CF}$ = 273.3 Hz), 149.6, 146.9 (d, $^{6}J_{CF}$ = 3.6 Hz), 139.1, 138.2 (d, $^{3}J_{CF}$ = 3.7 Hz), 135.2, 131.3, 130.4 (2C), 129.6 (d, $^{4}J_{CF}$ = 7.9 Hz, 2C), 129.2 (2C), 123.8 (2C), 111.7, 109.6 (d, $^{2}J_{CF}$ = 6.1 Hz), 49.0 (d, $^{2}J_{CF}$ = 28.0 Hz), 12.4; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –105.6 (dt, $^{3}J_{FH\textit{trans}}$ = 36.7 Hz, $^{3}J_{FH}$ = 17.4 Hz); MS (ESI) *m/z* 410 [M +

H]$^+$ (73), 105 (100); HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{21}H_{17}FN_3O_5$ 410.1152, found 410.1149. (*E*)-**19a**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 8.20–8.18 (m, 2H), 7.92–7.90 (m, 2H), 7.68–7.63 (m, 1H), 7.55 (d, $^3J_{HH}$ = 8.5 Hz, 2H), 7.51–7.48 (m, 2H), 7.13 (m, 1H), 6.56 (d, $^3J_{HF\textit{cis}}$ = 20.5 Hz, 1H), 4.70 (d, $^3J_{HF}$ = 17.4 Hz, 2H), 1.97 (d, $^4J_{HH}$ = 1.2 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.6, 162.8, 155.3 (d, $^1J_{CF}$ = 258.1 Hz), 149.6, 147.2, 139.6, 138.4 (d, $^3J_{CF}$ = 13.1 Hz), 135.2, 131.3, 130.5 (2C), 129.5 (d, $^4J_{CF}$ = 2.6 Hz, 2C), 129.2 (2C), 124.0 (2C), 111.8 (d, $^2J_{CF}$ = 27.2 Hz), 111.5, 45.4 (d, $^2J_{CF}$ = 26.2 Hz), 12.4; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –103.8 (dt, $^3J_{FH\textit{cis}}$ = 20.5 Hz, $^3J_{FH}$ = 17.4 Hz, 1F); MS (ESI) *m/z* 410 [M + H]$^+$ (73), 105 (100); HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{21}H_{17}FN_3O_5$ 410.1152, found 410.1149.

**(*Z*/*E*)-1-[3-(Anthracen-9-yl)-2-fluoroprop-2-en-1-yl]-3-benzoyl-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (20a).** General procedure C was followed with aminosulfone **6** (100 mg, 0.21 mmol, 1 equiv), 9-anthraldehyde (46 mg, 0.22 mmol, 1.05 equiv) and NaHMDS (1 M in THF, 0.32 mL, 0.32 mmol, 1.5 equiv) in THF (2 mL). The purification by flash chromatography ($CH_2Cl_2$, 100%) afforded compound **20a** (80 mg, 82%) as a yellow oil (*E*/*Z* = 17:83). (*Z*)-**20a**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 8.45 (s, 1H), 8.02–7.98 (m, 6H), 7.68–7.63 (m, 1H), 7.50–7.41 (m, 6H), 7.26 (m, 1H), 6.72 (d, $^3J_{HF\textit{trans}}$ = 36.6 Hz, 1H), 4.76 (d, $^3J_{HF}$ = 16.9 Hz, 2H), 1.95 (d, $^4J_{HH}$ = 1.1 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.8, 162.9, 153.4 (d, $^1J_{CF}$ = 263.0 Hz), 149.7, 139.6, 135.0, 131.4 (2C), 131.1, 130.4 (2C), 129.4, 129.2 (2C), 128.7 (2C), 127.6, 126.0 (2C), 125.4 (2C), 125.2 (2C), 124.6 (2C), 111.4, 107.9 (d, $^2J_{CF}$ = 12.4 Hz), 49.1 (d, $^2J_{CF}$ = 29.9 Hz), 12.3; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –107.4 (dt, $^3J_{FH\textit{trans}}$ = 36.6 Hz, $^3J_{FH}$ = 16.9 Hz, 1F); MS (ESI) *m/z* 465 [M + H]$^+$ (100), 235 (72), 105 (21); HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{29}H_{22}FN_2O_3$ 465.1614, found 465.1623. (*E*)-**20a**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 8.52 (s, 1H), 8.10–8.05 (m, 4H), 7.81–7.79 (m, 2H), 7.62–7.52 (m, 5H), 7.50–7.41 (m, 2H), 7.07 (d, $^3J_{HF\textit{cis}}$ = 15.6 Hz, 1H), 6.22 (m, 1H), 4.18 (d, $^3J_{HF}$ = 16.5 Hz, 2H), 1.57 (d, $^4J_{HH}$ = 1.1 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.6, 162.6, 156.2 (d, $^1J_{CF}$ = 261.2 Hz), 149.5, 138.6, 134.9, 131.4 (2C), 131.3, 130.3 (2C), 129.5, 129.1 (4C), 128.1, 126.8 (2C), 125.6 (2C), 124.9 (2C), 124.4 (2C), 110.8, 108.8 (d, $^2J_{CF}$ = 22.6 Hz), 44.8 (d, $^2J_{CF}$ = 30.6 Hz), 12.1; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –103.7 (dt, $^3J_{FH\textit{cis}}$ = 15.6 Hz, $^3J_{FH}$ = 16.5 Hz, 1F); MS (ESI) *m/z* 465 [M + H]$^+$ (100), 235 (72), 105 (21); HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{29}H_{22}FN_2O_3$ 465.1614, found 465.1623.

**(*Z*/*E*)-3-Benzoyl-1-[2-fluoro-3-(pyridin-3-yl)prop-2-en-1-yl]-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (21a).** General procedure C was followed with aminosulfone **6** (100 mg, 0.21 mmol, 1 equiv), 3-pyridinecarboxaldehyde (21 μL, 0.22 mmol, 1.05 equiv) and NaHMDS (1 M in THF, 0.32 mL, 0.32 mmol, 1.5 equiv) in THF (2 mL). The

purification by flash chromatography ($CH_2Cl_2$/AcOEt, 1:1) afforded compound **21a** (47 mg, 61%) as a colorless oil (*E*/*Z* = 16:84). $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 8.64 (s, 2H, *Z* and *E*), 8.49–8.48 (m, 2H, *Z* and *E*), 7.92–7.88 (m, 4H, *Z* and *E*), 7.85 (d, $^3J_{HH}$ = 8.0 Hz, 1H, *Z*), 7.75 (d, $^3J_{HH}$ = 8.0 Hz, 1H, *E*), 7.65–7.61 (m, 2H, *Z* and *E*), 7.49–7.45 (m, 4H, *Z* and *E*), 7.29–7.26 (m, 2H, *Z* and *E*), 7.22 (m, 1H, *Z*), 7.11 (m, 1H, *E*), 6.48 (d, $^3J_{HF\textit{cis}}$ = 19.7 Hz, 1H, *E*), 5.87 (d, $^3J_{HF\textit{trans}}$ = 38.1 Hz, 1H, *Z*), 4.66 (d, $^3J_{HF}$ = 17.2 Hz, 2H, *E*), 4.57 (d, $^3J_{HF}$ = 17.6 Hz, 2H, *Z*), 1.95 (m, 3H, *Z*), 1.93 (m, 3H, *E*); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.7 (*Z*), 168.6 (*E*), 162.8 (2C, *Z* and *E*), 154.8 (d, $^1J_{CF}$ = 256.9 Hz, *E*), 154.3 (d, $^1J_{CF}$ = 269.2 Hz, *Z*), 149.7 (d, $^4J_{CF}$ = 6.7 Hz, 2C, *Z* and *E*), 149.6 *Z*, 149.5 (*E*), 149.4 (d, $^6J_{CF}$ = 2.8 Hz, *E*), 148.8 (d, $^6J_{CF}$ = 2.5 Hz, *Z*), 139.5 (*E*), 139.1 (*Z*), 135.7 (d, $^4J_{CF}$ = 8.9 Hz, 2C, *Z* and *E*), 135.1 (2C, *Z* and *E*), 131.3 (*E*), 131.2 (*Z*), 130.4 (2C, *Z* and *E*), 130.3 (2C, *Z* and *E*), 129.1 (4C, *Z* and *E*), 127.9 (d, $^3J_{CF}$ = 3.2 Hz, *Z*), 127.8 (d, $^3J_{CF}$ = 5.1 Hz, *Z*), 123.6 (*E*), 123.5 (*Z*), 111.5 (*Z*), 111.3 (*E*), 109.9 (d, $^2J_{CF}$ = 26.3 Hz, *E*), 108.1 (d, $^2J_{CF}$ = 6.4 Hz, *Z*), 48.8 (d, $^2J_{CF}$ = 28.4 Hz, *Z*), 45.1 (d, $^2J_{CF}$ = 25.6 Hz, *E*), 12.4 (2C, *Z* and *E*); $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –105.5 (dt, $^3J_{FH}$ = 17.2 Hz, $^3J_{FH\textit{cis}}$ = 19.7 Hz, 1F, *E*), –108.2 (dt, $^3J_{FH\textit{trans}}$ = 38.1 Hz, $^3J_{FH}$ = 17.6 Hz, 1F, *Z*); MS (ESI) *m/z* 366 [M + H]$^+$ (32), 105 (100); HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{20}H_{17}FN_3O_3$ 366.1254, found 366.1262.

**(*Z*/*E*)-3-Benzoyl-1-(3-cyclohexyl-2-fluoroprop-2-en-1-yl)-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (22a).** General procedure C was followed with aminosulfone **6** (100 mg, 0.21 mmol, 1 equiv), cyclohexanecarboxaldehyde (27 μL, 0.22 mmol, 1.05 equiv) and NaHMDS (1 M in THF, 0.32 mL, 0.32 mmol, 1.5 equiv) in THF (2 mL). The purification by flash chromatography (pentane/AcOEt, 8:2) afforded compound **22a** (65 mg, 83%) as a colorless oil (*E*/*Z* = 28:72). $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.91–7.89 (m, 4H, *E* and *Z*), 7.65–7.62 (m, 2H, *E* and *Z*), 7.50–7.46 (m, 4H, *E* and *Z*), 7.14 (m, 2H, *E* and *Z*), 5.25 (dd, $^3J_{HF\textit{cis}}$ = 21.2 Hz, $^3J_{HH}$ = 10.8 Hz, 1H, *E*), 4.85 (dd, $^3J_{HF\textit{trans}}$ = 37.1 Hz, $^3J_{HH}$ = 9.3 Hz, 1H, *Z*), 4.51 (d, $^3J_{HF}$ = 20.1 Hz, 2H, *E*), 4.36 (d, $^3J_{HF}$ = 17.4 Hz, 2H, *Z*), 2.50–2.41 (m, 1H, *Z*), 2.35–2.29 (m, 1H, *E*), 1.96 (d, $^4J_{HH}$ = 1.1 Hz, 3H, *Z*), 1.91 (d, $^4J_{HH}$ = 2.6 Hz, 3H, *E*), 1.79–1.63 (m, 6H, *Z* and *E*), 1.49–1.40 (m, 2H, *Z* and *E*), 1.40–1.00 (m, 10H, *Z* and *E*), 0.90–0.83 (m, 2H, *Z* and *E*); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.8 (*E*), 168.7 (*Z*), 163.0 (*E*), 162.9 (*Z*), 151.3 (d, $^1J_{CF}$ = 247.4 Hz, *E*), 150.7 (d, $^1J_{CF}$ = 254.1 Hz, *Z*), 149.5 (*E*), 149.4 (*Z*), 139.4 (*E*), 138.9 (*Z*), 135.0 (2C, *E* and *Z*), 131.4 (2C, *Z* and *E*), 130.4 (2C, *E*), 130.3 (2C, *Z*), 129.1 (4C, *E* and *Z*), 118.3 (d, $^2J_{CF}$ = 15.1 Hz, *E*), 118.1 (d, $^2J_{CF}$ = 12.8 Hz, *Z*), 111.0 (*Z*), 110.9 (*E*), 48.1 (d, $^2J_{CF}$ = 30.2 Hz, *Z*), 44.3 (d, $^2J_{CF}$ = 28.6 Hz, *E*), 34.8 (d, $^4J_{CF}$ = 6.4 Hz, *E*), 33.5 (d, $^3J_{CF}$ = 2.2 Hz, *E*), 33.4 (d, $^3J_{CF}$ = 2.4 Hz, *Z*), 32.6 (d, $^4J_{CF}$ = 1.2 Hz, *Z*), 29.6 (*E*), 28.7 (*Z*), 25.7 (*Z*), 25.5

(2C, *Z*), 25.4 (*E*), 25.3 (2C, *E*), 12.4 (2C, *E* and *Z*); $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –113.5 (dt, $^3J_{FHcis}$ = 21.2 Hz, $^3J_{FH}$ = 20.1 Hz, 1F, *E*), –118.4 (dt, $^3J_{FHtrans}$ = 37.1 Hz, $^3J_{FH}$ = 17.4 Hz, 1F, *Z*); MS (EI) *m/z* 371 $[M + H]^+$ (84), 105 (100); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{21}H_{24}FN_2O_3$ 371.1771, found 371.1786.

**(*Z*/*E*)-3-Benzoyl-1-(2-fluorobut-2-en-1-yl)-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (23a).** General procedure C was followed with aminosulfone **6** (150 mg, 0.32 mmol, 1 equiv), acetaldehyde (19 µL, 0.33 mmol, 1.05 equiv) and NaHMDS (1 M in THF, 0.48 mL, 0.48 mmol, 1.5 equiv) in THF (3 mL). The purification by flash chromatography (pentane/AcOEt, 6:4) afforded compound **23a** (84 mg, 88%) as a colorless oil (*E*/*Z* = 41:59). $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.91–7.89 (m, 4H, *E* and *Z*), 7.64–7.61 (m, 2H, *E* and *Z*), 7.49–7.45 (m, 4H, *E* and *Z*), 7.16 (s, 2H, *E* and *Z*), 5.39 (dq, $^3J_{HFcis}$ = 20.6 Hz, $^3J_{HH}$ = 7.1 Hz, 1H, *E*), 4.99 (dq, $^3J_{HFtrans}$ = 36.3 Hz, $^3J_{HH}$ = 7.1 Hz, 1H, *Z*), 4.47 (d, $^3J_{HF}$ = 20.2 Hz, 2H, *E*), 4.35 (d, $^3J_{HF}$ = 17.4 Hz, 2H, *Z*), 1.92 (s, 6H, *E* and *Z*), 1.67 (dd, $^3J_{HH}$ = 7.1 Hz, $^4J_{HF}$ = 2.0 Hz, 3H, *E*), 1.63 (m, 3H, *Z*); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.9 (2C, *E* and *Z*), 163.0 (*E*), 162.9 (*Z*), 152.8 (d, $^1J_{CF}$ = 253.9 Hz, *Z*), 152.7 (d, $^1J_{CF}$ = 244.2 Hz, *E*), 149.5 (2C, *E* and *Z*), 139.7 (*E*), 139.3 (*Z*), 135.0 (*E*), 134.9 (*Z*), 131.4 (*Z*), 131.3 (*E*), 130.3 (2C, *E*), 130.2 (2C, *Z*), 129.1 (4C, *E* and *Z*), 110.9 (*Z*), 110.8 (*E*), 107.1 (d, $^2J_{CF}$ = 20.8 Hz, *E*), 106.7 (d, $^2J_{CF}$ = 13.4 Hz, *Z*), 48.0 (d, $^2J_{CF}$ = 29.9 Hz, *Z*), 43.9 (d, $^2J_{CF}$ = 28.7 Hz, *E*), 12.3 (2C, *E* and *Z*), 10.2 (d, $^3J_{CF}$ = 7.9 Hz, *E*), 8.9 (d, $^3J_{CF}$ = 5.5 Hz, *Z*); $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –112.2 (dt, $^3J_{FHcis}$ = 20.6 Hz, $^3J_{FH}$ = 20.2 Hz, 1F, *E*), –119.2 (dt, $^3J_{FHtrans}$ = 36.3 Hz, $^3J_{FH}$ = 17.4 Hz, 1F, *Z*); MS (ESI) *m/z* 303 $[M + H]^+$ (80), 105 (100); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{16}H_{16}FN_2O_3$ 303.1145, found 303.1134.

**(*Z*/*E*)-3-Benzoyl-1-(2-fluorononen-2-en-1-yl)-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (24a).** General procedure C was followed with aminosulfone **6** (100 mg, 0.21 mmol, 1 equiv), heptanal (31 µL, 0.22 mmol, 1.05 equiv) and NaHMDS (1 M in THF, 0.32 mL, 0.32 mmol, 1.5 equiv) in THF (2 mL). The purification by flash chromatography (pentane/AcOEt, 7:3) afforded compound **24a** (48 mg, 61%) as a colorless oil (*E*/*Z* = 29:71). (*Z*)-**24a**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.93–7.90 (m, 2H), 7.66–7.62 (m, 1H), 7.50–7.46 (m, 2H), 7.14 (t, $^4J_{HF}$ = 1.1 Hz, 1H), 4.97 (dt, $^3J_{HFtrans}$ = 36.8 Hz, $^3J_{HH}$ = 7.7 Hz, 1H), 4.38 (d, $^3J_{HF}$ = 17.4 Hz, 2H), 2.12 (q, $^3J_{HH}$ = 7.7 Hz, 2H), 1.97 (d, $^4J_{HH}$ = 1.1 Hz, 3H), 1.38–1.25 (m, 8H), 0.88 (t, $^3J_{HH}$ = 7.7 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.8, 163.0, 152.0 (d, $^1J_{CF}$ = 253.5 Hz), 149.6, 139.0, 135.0, 131.5, 130.4 (2C), 129.1 (2C), 112.6 (d, $^2J_{CF}$ = 12.9 Hz), 111.1, 48.2 (d, $^2J_{CF}$ = 30.0 Hz), 31.5, 28.8 (d, $^4J_{CF}$ = 1.7 Hz), 28.7, 23.6 (d, $^3J_{CF}$ = 3.7 Hz), 22.5, 14.0, 12.5; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –118.4 (dt, $^3J_{FHtrans}$ = 36.8 Hz, $^3J_{FH}$ = 17.4 Hz, 1F); MS (ESI) *m/z* 373 [M

+ H]$^+$ (100), 105 (97); HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{21}H_{26}FN_2O_3$ 373.1927, found 373.1928. (*E*)-**24a**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.93–7.90 (m, 2H), 7.66–7.62 (m, 1H), 7.51–7.47 (m, 2H), 7.15 (t, $^4J_{HF}$ = 1.2 Hz, 1H), 5.39 (dt, $^3J_{HFcis}$ = 21.1 Hz, $^3J_{HH}$ = 7.7 Hz, 1H), 4.50 (d, $^3J_{HF}$ = 20.6 Hz, 2H), 2.09 (q, $^3J_{HH}$ = 7.7 Hz, 2H), 1.96 (d, $^4J_{HH}$ = 1.2 Hz, 3H), 1.36–1.23 (m, 8H), 0.85 (t, $^3J_{HH}$ = 7.7 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.8, 163.0, 152.3 (d, $^1J_{CF}$ = 246.1 Hz), 149.6, 139.3, 135.0, 131.5, 130.5 (2C), 129.1 (2C), 112.8 (d, $^2J_{CF}$ = 18.2 Hz), 111.0, 44.1 (d, $^2J_{CF}$ = 27.3 Hz), 31.5, 29.6 (d, $^4J_{CF}$ = 2.3 Hz), 28.6, 25.2 (d, $^3J_{CF}$ = 7.5 Hz), 22.5, 14.0, 12.4; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –111.9 (dt, $^3J_{FHcis}$ = 21.1 Hz, $^3J_{FH}$ = 20.6 Hz, 1F); MS (ESI) *m/z* 373 [M + H]$^+$ (100), 105 (97); HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{21}H_{26}FN_2O_3$ 373.1927, found 373.1928.

**(*Z*/*E*)-3-Benzoyl-1-(2-fluoroundec-2-en-1-yl)-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (25a).** General procedure C was followed with aminosulfone **6** (100 mg, 0.21 mmol, 1 equiv), nonanal (38 μL, 0.22 mmol, 1.05 equiv) and NaHMDS (1 M in THF, 0.32 mL, 0.32 mmol, 1.5 equiv) in THF (2 mL). The purification by flash chromatography ($CH_2Cl_2$, 100%) afforded compound **25a** (44 mg, 52%) as a colorless oil (*E*/*Z* = 30:70). (*Z*)-**25a**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.93–7.90 (m, 2H), 7.66–7.62 (m, 1H), 7.51–7.47 (m, 2H), 7.15 (t, $^4J_{HH}$ = 1.0 Hz, 1H), 4.98 (dt, $^3J_{HFtrans}$ = 36.8 Hz, $^3J_{HH}$ = 7.5 Hz, 1H), 4.38 (d, $^3J_{HF}$ = 17.8 Hz, 2H), 2.12 (q, $^3J_{HH}$ = 7.5 Hz, 2H), 1.97 (d, $^4J_{HH}$ = 1.0 Hz, 3H), 1.39–1.26 (m, 12H), 0.88 (t, $^3J_{HH}$ = 7.5 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.8, 163.0, 152.0 (d, $^1J_{CF}$ = 253.0 Hz), 149.6, 139.0, 135.0, 131.5, 130.4 (2C), 129.1 (2C), 112.6 (d, $^2J_{CF}$ = 13.5 Hz), 111.1, 48.2 (d, $^2J_{CF}$ = 30.2 Hz), 31.8, 29.3, 29.2, 29.1, 28.8, 23.6 (d, $^3J_{CF}$ = 3.1 Hz), 22.6, 14.1, 12.4; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –118.4 (dt, $^3J_{FHtrans}$ = 36.8 Hz, $^3J_{FH}$ = 17.8 Hz, 1F); MS (ESI) *m/z* 401 [M + H]$^+$ (45), 105 (100); HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{23}H_{30}FN_2O_3$ 401.2240, found 401.2243. (*E*)-**25a**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.92–7.90 (m, 2H), 7.66–761 (m, 1H), 7.50–7.46 (m, 2H), 7.14 (t, $^4J_{HH}$ = 1.2 Hz, 1H), 5.39 (dt, $^3J_{HFcis}$ = 20.9 Hz, $^3J_{HH}$ = 7.5 Hz, 1H), 4.49 (d, $^3J_{HF}$ = 20.6 Hz, 2H), 2.09 (q, $^3J_{HH}$ = 7.5 Hz, 2H), 1.96 (d, $^4J_{HH}$ = 1.2 Hz, 3H), 1.36–1.22 (m, 12H), 0.86 (t, $^3J_{HH}$ = 7.5 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.8, 163.0, 152.3 (d, $^1J_{CF}$ = 246.2 Hz), 149.6, 139.3, 135.0, 131.5, 130.5 (2C), 129.1 (2C), 112.9 (d, $^2J_{CF}$ = 18.5 Hz), 111.1, 44.1 (d, $^2J_{CF}$ = 28.3 Hz), 31.8, 29.6, 29.3, 29.2, 29.0, 25.2 (d, $^3J_{CF}$ = 7.4 Hz), 22.6, 14.1, 12.4; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –111.9 (dt, $^3J_{FHcis}$ = 20.9 Hz, $^3J_{FH}$ = 20.6 Hz, 1F); MS (ESI) *m/z* 401 [M + H]$^+$ (45), 105 (100); HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{23}H_{30}FN_2O_3$ 401.2240, found 401.2243.

**General procedure E: preparation of fluorinated allylamines derived from thymine.** To a solution of aminosulfone **6** (1 equiv), and aldehyde (1.05 equiv) at –78 °C in THF (0.1 M)

was added NaHMDS (1 M in THF, 1.5 equiv). After 30 min at –78 °C, the mixture was stirred for 1 h 30 at 20 °C, quenched with a saturated aqueous solution of $NH_4Cl$ and extracted with $CH_2Cl_2$. Combined organic layers were washed with brine, dried over $MgSO_4$, filtered and evaporated under reduced pressure. To the crude mixture of fluoroallylamine derived from $N^3$-benzoyl-thymine **17a-30a** was added a methanolic solution of NaOH (1% in MeOH) and stirred 16 h at 20 °C. The solution was neutralized by the addition of 1N HCl and then concentrated. The crude product was purified by flash chromatography to give amino-alkenes **17b-30b**.

**(*Z*/*E*)-1-[2-Fluoro-3-(4-methoxyphenyl)prop-2-en-1-yl]-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (17b).** General procedure E was followed with aminosulfone **6** (200 mg, 0.42 mmol, 1 equiv), *p*-methoxybenzaldehyde (54 µL, 0.44 mmol, 1.05 equiv) and NaHMDS (1 M in THF, 0.63 mL, 0.63 mmol, 1.5 equiv) in THF (4 mL). The crude mixture was treated with a solution of NaOH in MeOH (5 mL). The purification by flash chromatography (pentane/AcOEt, 4:6) afforded compound **17b** (94 mg, 76%) as a yellow solid (*E*/*Z* = 7:93). Mp > 250 °C; (*Z*)-**17b**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 8.72 (sbr, 1H), 7.45–7.43 (m, 2H), 7.11 (m, 1H), 6.88–6.86 (m, 2H), 5.81 (d, $^3J_{HFtrans}$ = 38.7 Hz, 1H), 4.52 (d, $^3J_{HF}$ = 17.3 Hz, 2H), 3.81 (s, 3H), 1.94 (d, $^4J_{HH}$ = 1.0 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 163.8, 159.4 (d, $^6J_{CF}$ = 3.1 Hz), 151.4 (d, $^1J_{CF}$ = 263.5 Hz), 150.6, 139.2, 130.3 (d, $^4J_{CF}$ = 7.6 Hz, 2C), 124.5 (d, $^3J_{CF}$ = 3.0 Hz), 114.0 (2C), 111.3, 110.8 (d, $^2J_{CF}$ = 6.9 Hz), 55.3, 48.7 (d, $^2J_{CF}$ = 29.6 Hz), 12.3; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –113.8 (dt, $^3J_{FHtrans}$ = 38.7 Hz, $^3J_{FH}$ = 17.3 Hz, 1F); MS (ESI) *m/z* 291 $[M + H]^+$ (86), 165 (100); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{15}H_{16}FN_2O_3$ 291.1145, found 291.1154. (*E*)-**17b**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 8.80 (sbr, 1H), 7.25–7.23 (m, 2H), 6.97 (s, 1H), 6.93–6.91 (m, 2H), 6.52 (d, $^3J_{HFcis}$ = 20.3 Hz, 1H), 4.69 (d, $^3J_{HF}$ = 18.2 Hz, 2H), 3.82 (s, 3H), 1.90 (s, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 163.8, 159.4, 153.1 (d, $^1J_{CF}$ = 252.1 Hz), 150.7, 139.2, 129.8 (d, $^4J_{CF}$ = 2.5 Hz, 2C), 123.9 (d, $^3J_{CF}$ = 12.0 Hz), 114.3 (2C), 113.4 (d, $^2J_{CF}$ = 25.4 Hz), 111.2, 55.3, 44.5 (d, $^2J_{CF}$ = 27.4 Hz), 12.4; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –110.0 (dt, $^3J_{FHcis}$ = 20.3 Hz, $^3J_{FH}$ = 18.2 Hz, 1F); MS (ESI) *m/z* 291 $[M + H]^+$ (86), 165 (100); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{15}H_{16}FN_2O_3$ 291.1145, found 291.1154.

**(*Z*/*E*)-1-[3-(4-Bromophenyl)-2-fluoroprop-2-en-1-yl)-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (18b).** General procedure E was followed with aminosulfone **6** (200 mg, 0.42 mmol, 1 equiv), *p*-bromobenzaldehyde (82 mg, 0.44 mmol, 1.05 equiv) and NaHMDS (1 M in THF, 0.63 mL, 0.63 mmol, 1.5 equiv) in THF (4 mL). The crude mixture was treated with a solution of NaOH in MeOH (5 mL). The purification by

flash chromatography ($CH_2Cl_2$/AcOEt, 7:3) afforded compound **18b** (79 mg, 55%) as a white solid (*E*/*Z* = 17:83). Mp 200 °C; (*Z*)-**18b**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 8.71 (sbr, 1H), 7.48–7.45 (m, 2H), 7.37–7.34 (m, 2H), 7.08 (t, $^4J_{HF}$ = 1.2 Hz, 1H), 5.81 (d, $^3J_{HF\textit{trans}}$ = 37.8 Hz, $^3J_{HH}$ = 7.5 Hz, 1H), 4.52 (d, $^3J_{HF}$ = 17.1 Hz, 2H), 1.94 (d, $^4J_{HH}$ = 1.2 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 163.7, 153.4 (d, $^1J_{CF}$ = 268.4 Hz), 150.5, 139.2, 131.8 (2C), 130.7 (d, $^6J_{CF}$ = 3.2 Hz), 130.4 (d, $^4J_{CF}$ = 7.4 Hz, 2C), 122.1 (d, $^3J_{CF}$ = 3.5 Hz), 111.5, 110.1 (d, $^2J_{CF}$ = 6.4 Hz), 48.7 (d, $^2J_{CF}$ = 29.7 Hz), 12.4; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –109.8 (dt, $^3J_{FH\textit{trans}}$ = 37.8 Hz, $^3J_{FH}$ = 17.1 Hz, 1F); MS (EI) *m/z* 340 $[M]^{+\bullet}$ (45), 338 (47), 215 (55), 213 (58), 134 (100); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{14}H_{13}BrFN_2O_2$ 339.0144, found 339.0154. (*E*)-**18b**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 8.79 (sbr, 1H), 7.53–7.51 (m, 2H), 7.24–7.22 (m, 2H), 6.96 (t, $^4J_{HF}$ = 1.2 Hz, 1H), 6.47 (d, $^3J_{HF\textit{cis}}$ = 20.2 Hz, 1H), 4.64 (d, $^3J_{HF}$ = 17.9 Hz, 2H), 1.92 (d, $^4J_{HF}$ = 1.2 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 163.8, 154.2 (d, $^1J_{CF}$ = 254.3 Hz), 150.6, 139.4, 132.0 (2C), 130.6 (d, $^6J_{CF}$ = 12.0 Hz), 130.3 (d, $^4J_{CF}$ = 2.8 Hz, 2C), 122.2, 112.5 (d, $^2J_{CF}$ = 26.1 Hz), 111.4, 44.7 (d, $^2J_{CF}$ = 26.8 Hz), 12.4; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –107.4 (dt, $^3J_{FH\textit{cis}}$ = 20.2 Hz, $^3J_{FH}$ = 17.9 Hz, 1F); MS (EI) *m/z* 340 $[M]^{+\bullet}$ (45), 338 (47), 215 (55), 213 (58), 134 (100); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{14}H_{13}BrFN_2O_2$ 339.0144, found 339.0154.

**(*Z*/*E*)-1-[3-(Anthracen-9-yl)-2-fluoroprop-2-en-1-yl]-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (20b).** General procedure E was followed with aminosulfone **6** (150 mg, 0.32 mmol, 1 equiv), 9-anthraldehyde (69 mg, 0.33 mmol, 1.05 equiv) and NaHMDS (1 M in THF, 0.47 mL, 0.47 mmol, 1.5 equiv) in THF (3 mL). The crude mixture was treated with a solution of NaOH in MeOH (5 mL). The purification by flash chromatography ($CH_2Cl_2$/AcOEt, 7:3) afforded compound **20b** (74 mg, 65%) as a yellow solid (*E*/*Z* = 15:85). Mp 198 °C; (*Z*)-**20b**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 8.70 (sbr, 1H), 8.44 (s, 1H), 8.02–7.99 (m, 4H), 7.51–7.44 (m, 4H), 7.20 (s, 1H), 6.72 (d, $^3J_{HF\textit{trans}}$ = 37.9 Hz, 1H), 4.78 (d, $^3J_{HF}$ = 15.8 Hz, 2H), 1.95 (s, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 163.9, 153.7 (d, $^1J_{CF}$ = 263.0 Hz), 150.6, 139.8, 131.2 (2C), 129.5, 128.8 (2C), 127.7, 126.1 (2C), 125.4 (2C), 125.2 (2C), 124.7 (2C), 111.5, 107.4 (d, $^2J_{CF}$ = 12.6 Hz), 48.7 (d, $^2J_{CF}$ = 30.3 Hz), 12.4; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –106.7 (dt, $^3J_{FH\textit{trans}}$ = 37.9 Hz, $^3J_{FH}$ = 15.8 Hz, 1F); MS (ESI) *m/z* 361 $[M + H]^+$ (44), 235 (100); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{22}H_{18}FN_2O_2$ 361.1352, found 361.1347. (*E*)-**20b**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 8.47 (s, 1H), 8.11–8.03 (m, 4H), 7.58–7.50 (m, 4H), 7.05 (d, $^3J_{HF\textit{cis}}$ = 17.4 Hz, 1H), 6.08 (s, 1H), 4.22 (d, $^3J_{HF}$ = 14.7 Hz, 2H), 1.45 (s, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 163.1, 156.3 (d, $^1J_{CF}$ = 259.2 Hz), 150.1, 138.9, 131.3 (2C), 130.3 (d, $^3J_{CF}$ = 1.7 Hz), 129.0 (2C), 127.8, 126.6 (2C), 125.6 (2C), 125.1 (2C), 124.5, 124.4, 110.4, 107.9 (d, $^2J_{CF}$ = 22.6 Hz), 45.0 (d, $^2J_{CF}$ = 33.0 Hz), 11.9;

$^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –102.8 (dt, $^3J_{FHcis}$ = 17.4 Hz, $^3J_{FH}$ = 14.7 Hz, 1F); MS (ESI) *m/z* 361 $[M + H]^+$ (44), 235 (100); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{22}H_{18}FN_2O_2$ 361.1352, found 361.1347.

**(*Z*/*E*)-1-[2-Fluoro-3-(pyridin-3-yl)prop-2-en-1-yl]-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (21b).** General procedure E was followed with aminosulfone **6** (200 mg, 0.42 mmol, 1 equiv), 3-pyridinecarboxaldehyde (42 μL, 0.44 mmol, 1.05 equiv) and NaHMDS (1 M in THF, 0.63 mL, 0.63 mmol, 1.5 equiv) in THF (4 mL). The crude mixture was treated with a solution of NaOH in MeOH (5 mL). The solution was neutralized by the addition of 1 N HCl and 1 M NaOH was added until pH 7. The aqueous layer was extracted with $CH_2Cl_2$. The combined organic layers were dried over $MgSO_4$, filtered and evaporated under reduced pressure. The purification by flash chromatography ($CH_2Cl_2$/MeOH, 95:5) afforded compound **21b** (73 mg, 66%) as a yellow solid (*E*/*Z* = 12:88). Mp 184 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 9.58 (sbr, 2H, *Z* and *E*), 8.67–8.49 (m, 4H, *Z* and *E*), 7.90–7.84 (m, 2H, *Z* and *E*), 7.38–7.36 (m, 1H, *E*), 7.31–7.27 (m, 1H, *Z*), 7.10 (s, 1H, *Z*), 7.0 (s, 1H, *E*), 6.47 (d, $^3J_{HFcis}$ = 19.6 Hz, 1H, *E*), 5.89 (d, $^3J_{HFtrans}$ = 38.0 Hz, 1H, *Z*), 4.64 (d, $^3J_{HF}$ = 17.6 Hz, 2H, *E*), 4.56 (d, $^3J_{HF}$ = 16.4 Hz, 2H, *Z*), 1.94 (s, 3H, *Z*), 1.91 (m, 3H, *E*); $^{13}$C NMR ($CDCl_3$, 100 MHz) (*Z*)-isomer $\delta$ 164.0, 154.9 (d, $^1J_{CF}$ = 269.1 Hz), 150.7, 149.4 (d, $^4J_{CF}$ = 7.0 Hz), 148.5 (d, $^6J_{CF}$ = 2.8 Hz), 139.2, 135.9 (d, $^4J_{CF}$ = 9.1 Hz), 128.2 (d, $^3J_{CF}$ = 2.8 Hz), 123.6, 111.6, 107.5 (d, $^2J_{CF}$ = 6.8 Hz), 48.5 (d, $^2J_{CF}$ = 29.7 Hz), 12.3; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –104.8 (dt, $^3J_{FH}$ = 19.6 Hz, $^3J_{FHcis}$ = 17.6 Hz, 1F, *E*), –107.6 (dt, $^3J_{FHtrans}$ = 38.0 Hz, $^3J_{FH}$ = 16.4 Hz, 1F, *Z*); MS (ESI) *m/z* 262 $[M + H]^+$ (100), 242 (33), 199 (63), 171 (23), 136 (85); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{13}H_{13}FN_3O_2$ 262.0992, found 262.0989.

**(*Z*/*E*)-1-(3-(Cyclohexyl-2-fluoroprop-2-en-1-yl)-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (22b).** General procedure E was followed with aminosulfone **6** (200 mg, 0.42 mmol, 1 equiv), cyclohexanecarboxaldehyde (54 μL, 0.44 mmol, 1.05 equiv) and NaHMDS (1 M in THF, 0.63 mL, 0.63 mmol, 1.5 equiv) in THF (4 mL). The crude mixture was treated with a solution of NaOH in MeOH (5 mL). The purification by flash chromatography ($CH_2Cl_2$/AcOEt, 8:2) afforded compound **22b** (64 mg, 57%) as a white solid (*E*/*Z* = 21:79). Mp 184 °C; (*Z*)-**22b**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 8.74 (sbr, 1H), 7.02 (s, 1H), 4.82 (dd, $^3J_{HFtrans}$ = 37.1 Hz, $^3J_{HH}$ = 9.4 Hz, 1H), 4.33 (d, $^3J_{HF}$ = 17.0 Hz, 2H), 2.48–2.39 (m, 1H), 1.92 (s, 3H), 1.69–1.66 (m, 4H), 1.34–1.03 (m, 6H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 163.9, 151.0 (d, $^1J_{CF}$ = 254.2 Hz), 150.5, 139.2, 117.6 (d, $^2J_{CF}$ = 12.7 Hz), 111.1, 47.8 (d, $^2J_{CF}$ = 31.8 Hz), 33.4 (d, $^3J_{CF}$ = 2.9 Hz), 32.7 (2C), 25.8, 25.6 (2C), 12.4; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –118.3 (dt, $^3J_{FHtrans}$ = 37.1 Hz, $^3J_{FH}$ = 17.0 Hz, 1F); MS (ESI) *m/z* 267 $[M + H]^+$ (100), 127

(98); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{14}H_{20}FN_2O_2$ 267.1509, found 267.1516. (*E*)-**22b**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 8.47 (sbr, 1H), 7.03 (s, 1H), 5.23 (dd, $^3J_{HFcis}$ = 21.3 Hz, $^3J_{HH}$ = 10.6 Hz, 1H), 4.47 (d, $^3J_{HF}$ = 20.4 Hz, 2H), 2.30–2.20 (m, 1H), 1.92 (s, 3H), 1.74–1.63 (m, 4H), 1.37–1.05 (m, 6H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 163.8, 151.5 (d, $^1J_{CF}$ = 246.9 Hz), 150.4, 139.6, 118.0 (d, $^2J_{CF}$ = 15.4 Hz), 110.9, 44.1 (d, $^2J_{CF}$ = 28.9 Hz), 35.0 (d, $^3J_{CF}$ = 6.8 Hz), 33.6, 33.5, 25.6, 25.5 (2C), 12.4; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –113.8 (dt, $^3J_{FHcis}$ = 21.3 Hz, $^3J_{FH}$ = 20.4 Hz, 1F); MS (ESI) *m/z* 267 $[M + H]^+$ (100), 127 (98); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{14}H_{20}FN_2O_2$ 267.1509, found 267.1516.

**(*Z*/*E*)-1-(2-Fluorobut-2-en-1-yl)-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (23b).** General procedure E was followed with aminosulfone **6** (200 mg, 0.42 mmol, 1 equiv), acetaldehyde (25 µL, 0.44 mmol, 1.05 equiv) and NaHMDS (1 M in THF, 0.63 mL, 0.63 mmol, 1.5 equiv) in THF (4 mL). The crude mixture was treated with a solution of NaOH in MeOH (5 mL). The purification by flash chromatography (pentane/AcOEt, 7:3) afforded compound **23b** (69 mg, 82%) as a white solid (*E*/*Z* = 39:61). Mp 114 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 10.02 (sbr, 1H, *E*), 9.96 (sbr, 1H, *Z*), 7.03–7.02 (m, 2H, *E* and *Z*), 5.35 (dq, $^3J_{HFcis}$ = 20.3 Hz, $^3J_{HH}$ = 7.4 Hz, 1H, *E*), 4.97 (dq, $^3J_{HFtrans}$ = 36.3 Hz, $^3J_{HH}$ = 7.0 Hz, 1H, *Z*), 4.44 (d, $^3J_{HF}$ = 20.6 Hz, 2H, *E*), 4.34 (d, $^3J_{HF}$ = 16.9 Hz, 2H, *Z*), 1.89 (s, 6H, *E* and *Z*), 1.71 (dd, $^3J_{HH}$ = 7.4 Hz, $^4J_{HF}$ = 2.2 Hz, 3H, *E*), 1.60 (dd, $^3J_{HH}$ = 7.0 Hz, $^4J_{HF}$ = 2.2 Hz, 3H, *Z*); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 164.5 (*E*), 164.4 (*Z*), 153.2 (d, $^1J_{CF}$ = 244.5 Hz, *Z*), 153.1 (d, $^1J_{CF}$ = 254.0 Hz, *E*), 151.0 *E*, 150.9 (*Z*), 139.6 (*E*), 139.3 (*Z*), 111.0 (*Z*), 110.9 (*E*), 106.8 (d, $^2J_{CF}$ = 20.7 Hz, *E*), 106.1 (d, $^2J_{CF}$ = 13.5 Hz, *Z*), 47.6 (d, $^2J_{CF}$ = 31.1 Hz, *Z*), 43.6 (d, $^2J_{CF}$ = 29.5 Hz, *E*), 12.2 (2C, *E* and *Z*), 10.3 (d, $^3J_{CF}$ = 8.8 Hz, *E*), 8.8 (d, $^3J_{CF}$ = 5.6 Hz, *Z*); $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –111.7 (dtq, $^3J_{FHcis}$ = 20.3 Hz, $^3J_{FH}$ = 20.6 Hz, $^4J_{FH}$ = 2.2 Hz, 1F, *E*), –118.8 (dtq, $^3J_{FHtrans}$ = 36.3 Hz, $^3J_{FH}$ = 16.9 Hz, $^4J_{FH}$ = 2.2 Hz, 1F, *Z*); MS (ESI) *m/z* 199 $[M + H]^+$ (33), 127 (100); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_9H_{12}FN_2O_2$ 199.0883, found 199.0886.

**(*Z*/*E*)-1-(2-Fluoronon-2-en-1-yl)-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (24b).** General procedure E was followed with aminosulfone **6** (200 mg, 0.42 mmol, 1 equiv), heptanal (62 µL, 0.44 mmol, 1.05 equiv) and NaHMDS (1 M in THF, 0.63 mL, 0.63 mmol, 1.5 equiv) in THF (4 mL). The crude mixture was treated with a solution of NaOH in MeOH (5 mL). The purification by flash chromatography (pentane/$Et_2O$, 4:6) afforded compound **24b** (76 mg, 67%) as a white solid (*E*/*Z* = 30:70). Mp 105 °C; (*Z*)-**24b**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 9.31 (sbr, 1H), 7.03 (t, $^4J_{HF}$ = 1.1 Hz, 1H), 4.95 (dt, $^3J_{HFtrans}$ = 36.7 Hz, $^3J_{HH}$ = 7.5 Hz, 1H), 4.36 (d, $^3J_{HF}$ = 16.9 Hz, 2H), 2.09 (q, $^3J_{HH}$ = 7.5 Hz, 2H), 1.92 (d, $^4J_{HH}$ = 1.1 Hz, 3H), 1.42–1.24 (m, 8H), 0.87 (t, $^3J_{HH}$ = 7.5 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 164.2, 152.3

(d, $^{1}J_{CF}$ = 254.2 Hz), 150.8, 139.3, 112.0 (d, $^{2}J_{CF}$ = 13.4 Hz), 111.1, 47.7 (d, $^{2}J_{CF}$ = 31.6 Hz), 31.5, 28.8 (d, $^{4}J_{CF}$ = 1.5 Hz), 28.7, 23.5 (d, $^{3}J_{CF}$ = 3.8 Hz), 22.5, 14.0, 12.3; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –118.2 (dt, $^{3}J_{FH\textit{trans}}$ = 36.7 Hz, $^{3}J_{FH}$ = 16.9 Hz, 1F); MS (ESI) *m/z* 269 [M + H]$^+$ (45), 127 (100); HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{14}H_{22}FN_2O_2$ 269.1665, found 269.1674. (*E*)-**24b**: $^{1}$H NMR ($CDCl_3$, 400 MHz) $\delta$ 9.12 (sbr, 1H), 7.04 (t, $^{4}J_{HF}$ = 1.2 Hz, 1H), 5.36 (dt, $^{3}J_{HF\textit{cis}}$ = 21.0 Hz, $^{3}J_{HH}$ = 7.4 Hz, 1H), 4.46 (d, $^{3}J_{HF}$ = 20.3 Hz, 2H), 2.12 (q, $^{3}J_{HH}$ = 7.4 Hz, 2H), 1.92 (d, $^{4}J_{HH}$ = 1.2 Hz, 3H), 1.40–1.25 (m, 8H), 0.87 (t, $^{3}J_{HH}$ = 7.4 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 164.2, 152.4 (d, $^{1}J_{CF}$ = 246.3 Hz), 150.7, 139.5, 112.5 (d, $^{2}J_{CF}$ = 17.4 Hz), 110.9, 43.8 (d, $^{2}J_{CF}$ = 29.4 Hz), 31.6, 29.6 (d, $^{4}J_{CF}$ = 1.9 Hz), 28.7, 25.2 (d, $^{3}J_{CF}$ = 7.4 Hz), 22.5, 14.0, 12.3; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –111.6 (dt, $^{3}J_{FH\textit{cis}}$ = 21.0 Hz, $^{3}J_{FH}$ = 20.3 Hz, 1F); MS (ESI) *m/z* 269 [M + H]$^+$ (45), 127 (100); HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{14}H_{22}FN_2O_2$ 269.1665, found 269.1674.

**(*Z*/*E*)-1-(2-Fluoroundec-2-en-1-yl)-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (25b).** General procedure E was followed with aminosulfone **6** (200 mg, 0.42 mmol, 1 equiv), nonanal (76 μL, 0.44 mmol, 1.05 equiv) and NaHMDS (1 M in THF, 0.63 mL, 0.63 mmol, 1.5 equiv) in THF (4 mL). The crude mixture was treated with a solution of NaOH in MeOH (5 mL). The purification by flash chromatography (pentane/$Et_2O$, 4:6) afforded compound **25b** (98 mg, 78%) as a colorless oil (*E*/*Z* = 28:72). (*Z*)-**25b**: $^{1}$H NMR ($CDCl_3$, 400 MHz) $\delta$ 9.06 (sbr, 1H), 7.02 (t, $^{4}J_{HH}$ = 1.0 Hz, 1H), 4.93 (dt, $^{3}J_{HF\textit{trans}}$ = 36.4 Hz, $^{3}J_{HH}$ = 7.5 Hz, 1H), 4.34 (d, $^{3}J_{HF}$ = 16.9 Hz, 2H), 2.08 (q, $^{3}J_{HH}$ = 7.5 Hz, 2H), 1.91 (d, $^{4}J_{HH}$ = 1.0 Hz, 3H), 1.36–1.24 (m, 12H), 0.86 (t, $^{3}J_{HH}$ = 7.5 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 164.3, 152.2 (d, $^{1}J_{CF}$ = 253.8 Hz), 150.8, 139.2, 111.9 (d, $^{2}J_{CF}$ = 13.0 Hz), 111.0, 47.7 (d, $^{2}J_{CF}$ = 31.1 Hz), 31.7, 29.2, 29.1, 29.0, 28.8 (d, $^{4}J_{CF}$ = 1.3 Hz), 23.5 (d, $^{3}J_{CF}$ = 3.7 Hz), 22.5, 14.0, 12.3; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –118.2 (dt, $^{3}J_{FH\textit{trans}}$ = 36.4 Hz, $^{3}J_{FH}$ = 16.9 Hz, 1F); MS (ESI) *m/z* 297 [M + H]$^+$ (51), 127 (100); HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{16}H_{26}FN_2O_2$ 297.1978, found 297.1976. (*E*)-**25b**: $^{1}$H NMR ($CDCl_3$, 400 MHz) $\delta$ 8.64 (sbr, 1H), 7.03 (t, $^{4}J_{HH}$ = 1.2 Hz, 1H), 5.36 (dt, $^{3}J_{HF\textit{cis}}$ = 21.0 Hz, $^{3}J_{HH}$ = 7.4 Hz, 1H), 4.45 (d, $^{3}J_{HF}$ = 20.5 Hz, 2H), 2.11 (q, $^{3}J_{HH}$ = 7.4 Hz, 2H), 1.91 (d, $^{4}J_{HH}$ = 1.2 Hz, 3H), 1.42–1.26 (m, 12H), 0.87 (t, $^{3}J_{HH}$ = 7.4 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 164.2, 152.5 (d, $^{1}J_{CF}$ = 246.6 Hz), 150.6, 139.5, 112.4 (d, $^{2}J_{CF}$ = 17.9 Hz), 110.9, 43.7 (d, $^{2}J_{CF}$ = 29.5 Hz), 31.7, 29.6 (d, $^{4}J_{CF}$ = 1.8 Hz), 29.3, 29.1, 29.0, 25.2 (d, $^{3}J_{CF}$ = 7.6 Hz), 22.6, 14.0, 12.3; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –111.7 (dt, $^{3}J_{FH\textit{cis}}$ = 21.0 Hz, $^{3}J_{FH}$ = 20.5 Hz, 1F); MS (ESI) *m/z* 297 [M + H]$^+$ (51), 127 (100); HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{16}H_{26}FN_2O_2$ 297.1978, found 297.1976.

**3-Benzoyl-1-[2-(2,2-dimethyl-1,3-dioxan-5-ylidene)-2-fluoroethyl]-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (26).** General procedure C was followed with aminosulfone **6** (100 mg, 0.21 mmol, 1 equiv), 2,2-dimethyl-1,3-dioxan-5-one (29 mg, 0.22 mmol, 1.05 equiv) and NaHMDS (1 M in THF, 0.32 mL, 0.32 mmol, 1.5 equiv) in THF (2 mL). The purification by flash chromatography (pentane/AcOEt, 1:1, 1% $Et_3N$) afforded compound **26** (50 mg, 60%) as a colorless oil. $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.92–7.89 (m, 2H), 7.66–7.63 (m, 1H), 7.51–7.47 (m, 2H), 7.15 (m, 1H), 4.45 (d, $^3J_{HF}$ = 2.4 Hz, 2H), 4.42 (d, $^3J_{HF}$ = 2.4 Hz, 2H), 4.41 (d, $^3J_{HF}$ = 21.5 Hz, 2H), 1.95 (d, $^4J_{HH}$ = 0.9 Hz, 3H), 1.38 (s, 6H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.7, 162.9, 149.5, 145.4 (d, $^1J_{CF}$ = 248.8 Hz), 139.6, 135.1, 131.3, 130.4 (2C), 129.1 (2C), 116.8 (d, $^2J_{CF}$ = 13.7 Hz), 111.2, 99.4, 57.8 (d, $^3J_{CF}$ = 8.2 Hz), 56.6 (d, $^3J_{CF}$ = 8.2 Hz), 44.9 (d, $^2J_{CF}$ = 28.7 Hz), 23.7 (2C), 12.3; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –118.8 (t, $^3J_{FH}$ = 21.5 Hz, 1F); MS (ESI) *m/z* 411 $[M + Na]^+$ (100), 264 (17), 252 (47); HRMS (ESI) *m/z* $[M + Na]^+$ calcd for $C_{20}H_{21}FN_2NaO_5$ 411.1332, found 411.1312.

**1-[2-Fluoro-4-hydroxy-3-(hydroxymethyl)but-2-en-1-yl]-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (27).** Dioxan **26** (95 mg, 0.24 mmol) was dissolved in a mixed solvent (THF/$H_2O$/AcOH = 1:1:1, 6 mL) at 20 °C and stirred overnight at the same temperature. After concentration in vacuo, the residue was purified by flash chromatography ($CH_2Cl_2$/MeOH, 94:6) to give the corresponding diol (74 mg, 88%) as a colorless oil. $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.90–7.88 (m, 2H), 7.67–7.63 (m, 1H), 7.51–7.47 (m, 2H), 7.21 (s, 1H), 4.54 (d, $^3J_{HF}$ = 21.5 Hz, 2H), 4.32 (s, 2H), 4.27 (s, 2H), 3.05 (sbr, 2H), 1.95 (s, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.7, 162.9, 151.1 (d, $^1J_{CF}$ = 255.1 Hz), 149.9, 140.3, 135.3, 131.1, 130.4 (2C), 129.2 (2C), 121.7 (d, $^2J_{CF}$ = 9.4 Hz), 111.4, 58.6 (d, $^3J_{CF}$ = 7.9 Hz), 57.1 (d, $^3J_{CF}$ = 9.4 Hz), 45.7 (d, $^2J_{CF}$ = 28.5 Hz), 12.2; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –114.05 (t, $^3J_{FH}$ = 21.4 Hz, 1F); MS (ESI) *m/z* 349 $[M + H]^+$ (46), 331 (42), 227 (100); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{17}H_{18}FN_2O_5$ 349.1200, found 349.1194.

To the solution of diol (74 mg, 0.21 mmol), was added a methanolic solution of NaOH (1% in MeOH) (3mL) and stirred 16 h at 20 °C. The solution was neutralized by the addition of 1N HCl and then concentrated. The crude product was purified by flash chromatography ($CH_2Cl_2$/MeOH, 94:6) to give compound **27** (33 mg, 63%) as a orange oil. $^1$H NMR (MeOD, 400 MHz) $\delta$ 7.46 (m, 1H), 4.67 (d, $^3J_{HF}$ = 21.1 Hz, 2H), 4.34 (d, $^4J_{HF}$ = 1.5 Hz, 2H), 4.25 (d, $^4J_{HF}$ = 2.9 Hz, 2H), 1.87 (d, $^4J_{HH}$ = 1.0 Hz, 3H); $^{13}$C NMR (MeOD, 100 MHz) $\delta$ 166.7, 154.0 (d, $^1J_{CF}$ = 255.8 Hz), 152.8, 142.6, 122.8 (d, $^2J_{CF}$ = 9.7 Hz), 111.5, 58.1 (d, $^3J_{CF}$ = 8.3 Hz), 56.2 (d, $^3J_{CF}$ = 9.9 Hz), 45.7 (d, $^2J_{CF}$ = 28.4 Hz), 12.2; $^{19}$F NMR (MeOD, 376 MHz) $\delta$ –116.9 (t,

$^3J_{FH}$ = 21.1 Hz, 1F); MS (ESI) *m/z* 245 $[M + H]^+$ (68), 227 (100); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{10}H_{14}FN_2O_4$ 245.0938, found 245.0927.

**(*Z*/*E*)-3-Benzoyl-1-[6-(benzyloxy)-2-fluorohex-2-en-1-yl]-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (28a).** General procedure C was followed with aminosulfone **6** (100 mg, 0.21 mmol, 1 equiv), 4-(benzyloxy)-butanal (40 mg, 0.22 mmol, 1.05 equiv) and NaHMDS (1 M in THF, 0.32 mL, 0.32 mmol, 1.5 equiv) in THF (2 mL). The purification by flash chromatography (pentane/AcOEt, 65:35) afforded compound **28a** (61 mg, 66%) as a colorless oil (*E*/*Z* = 32:68). (*Z*)-**28a**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.92–7.90 (m, 2H), 7.65–7.61 (m, 1H), 7.50–7.46 (m, 2H), 7.37–7.26 (m, 5H), 7.12 (m, 1H), 4.99 (dt, $^3J_{HF\textit{trans}}$ = 36.4 Hz, $^3J_{HH}$ = 7.6 Hz, 1H), 4.49 (s, 2H), 4.37 (d, $^3J_{HF}$ = 17.3 Hz, 2H), 3.47 (t, $^3J_{HH}$ = 7.6 Hz, 2H), 2.24 (q, $^3J_{HH}$ = 7.6 Hz, 2H), 1.95 (d, $^4J_{HH}$ = 0.9 Hz, 3H), 1.70 (quint, $^3J_{HH}$ = 7.6 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.8, 162.9, 152.4 (d, $^1J_{CF}$ = 256.8 Hz), 149.6, 139.0, 138.4, 135.0, 131.5, 130.4 (2C), 129.1 (2C), 128.3 (2C), 127.6 (2C), 127.5, 111.8 (d, $^2J_{CF}$ = 14.6 Hz), 111.1, 72.9, 69.4, 48.1 (d, $^2J_{CF}$ = 29.2 Hz), 28.9, 20.6 (d, $^3J_{CF}$ = 4.0 Hz), 12.4; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –117.7 (dt, $^3J_{FH\textit{trans}}$ = 36.4 Hz, $^3J_{FH}$ = 17.3 Hz, 1F); MS (EI) *m/z* 437 $[M + H]^+$ (100), 331 (47), 105 (37); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{25}H_{26}FN_2O_4$ 437.1877, found 437.1885. (*E*)-**28a**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.93–7.90 (m, 2H), 7.66–7.61 (m, 1H), 7.50–7.46 (m, 2H), 7.34–7.25 (m, 5H), 7.13 (t, $^4J_{HH}$ = 1.1 Hz, 1H), 5.39 (dt, $^3J_{HF\textit{cis}}$ = 20.6 Hz, $^3J_{HH}$ = 7.4 Hz, 1H), 4.47 (d, $^3J_{HF}$ = 20.8 Hz, 2H), 4.45 (s, 2H), 3.45 (t, $^3J_{HH}$ = 7.4 Hz, 2H), 2.23 (q, $^3J_{HH}$ = 7.4 Hz, 2H), 1.95 (d, $^4J_{HH}$ = 1.1 Hz, 3H), 1.68 (quint, $^3J_{HH}$ = 7.4 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.8, 163.0, 152.7 (d, $^3J_{HH}$ = 7.4 Hz), 149.6, 139.4, 138.3, 135.0, 131.5, 130.4 (2C), 129.1 (2C), 128.4, 128.3, 127.6 (2C), 127.5, 112.0 (d, $^2J_{CF}$ = 20.7 Hz), 111.0, 72.8, 68.9, 44.1 (d, $^2J_{CF}$ = 28.5 Hz), 29.4 (d, $^4J_{CF}$ = 2.2 Hz), 22.0 (d, $^3J_{CF}$ = 7.9 Hz), 12.4; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –111.6 (dt, $^3J_{FH\textit{cis}}$ = 20.6 Hz, $^3J_{FH}$ = 20.8 Hz, 1F); MS (EI) *m/z* 437 $[M + H]^+$ (100), 331 (47), 105 (37); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{25}H_{26}FN_2O_4$ 437.1877, found 437.1885.

**(*Z*/*E*)-3-Benzoyl-1-[7-(benzyloxy)-2-fluorohept-2-en-1-yl]-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (29a).** General procedure C was followed with aminosulfone **6** (100 mg, 0.21 mmol, 1 equiv), 5-(benzyloxy)-pentanal (43 mg, 0.22 mmol, 1.05 equiv) and NaHMDS (1 M in THF, 0.32 mL, 0.32 mmol, 1.5 equiv) in THF (2 mL). The purification by flash chromatography (pentane/AcOEt, 65:35) afforded compound **29a** (49 mg, 52%) as a colorless oil (*E*/*Z* = 29:71). (*Z*)-**29a**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.92–7.90 (m, 2H), 7.65–7.61 (m, 1H), 7.50–7.46 (m, 2H), 7.37–7.28 (m, 5H), 7.13 (m, 1H), 4.98 (dt,

$^3J_{HFtrans}$ = 36.3 Hz, $^3J_{HH}$ = 7.5 Hz, 1H), 4.49 (s, 2H), 4.38 (d, $^3J_{HF}$ = 17.3 Hz, 2H), 3.47 (t, $^3J_{HH}$ = 6.3 Hz, 2H), 2.16 (q, $^3J_{HH}$ = 6.3 Hz, 2H), 1.97 (d, $^4J_{HH}$ = 1.1 Hz, 3H), 1.63 (quint, $^3J_{HH}$ = 6.3 Hz, 2H), 1.48 (quint, $^3J_{HH}$ = 6.3 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.8, 162.9, 152.2 (d, $^1J_{CF}$ = 256.0 Hz), 149.6, 139.0, 138.5, 135.0, 131.5, 130.4 (2C), 129.1 (2C), 128.3 (2C), 127.6 (2C), 127.5, 112.2 (d, $^2J_{CF}$ = 13.7 Hz), 111.2, 72.9, 69.9, 48.2 (d, $^2J_{CF}$ = 29.7 Hz), 29.2, 25.6, 23.5, 12.4; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –118.0 (dt, $^3J_{FHtrans}$ = 36.3 Hz, $^3J_{FH}$ = 17.3 Hz, 1F); MS (ESI) *m/z* 451 $[M + H]^+$ (100), 329 (77), 195 (21), 105 (24), 91 (40); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{26}H_{28}FN_2O_4$ 451.2033, found 451.2047. (*E*)-**29a**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.92–7.90 (m, 2H), 7.65–7.60 (m, 1H), 7.50–7.46 (m, 2H), 7.35–7.25 (m, 5H), 7.13 (t, $^4J_{HH}$ = 1.1 Hz, 1H), 5.38 (dt, $^3J_{HFcis}$ = 20.8 Hz, $^3J_{HH}$ = 7.6 Hz, 1H), 4.46 (d, $^3J_{HF}$ = 20.6 Hz, 2H), 4.46 (s, 2H), 3.43 (t, $^3J_{HH}$ = 6.3 Hz, 2H), 2.13 (q, $^3J_{HH}$ = 7.6 Hz, 2H), 1.96 (d, $^4J_{HH}$ = 1.1 Hz, 3H), 1.62–1.55 (m, 2H), 1.50–1.42 (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.8, 163.0, 152.5 (d, $^1J_{CF}$ = 246.8 Hz), 149.6, 139.4, 138.5, 135.0, 131.5, 130.4 (2C), 129.1 (2C), 128.3 (2C), 127.6 (2C), 127.5, 112.4 (d, $^2J_{CF}$ = 18.3 Hz), 111.0, 72.9, 70.0, 44.1 (d, $^2J_{CF}$ = 29.7 Hz), 29.0, 26.4 (d, $^4J_{CF}$ = 2.3 Hz), 25.0 (d, $^3J_{CF}$ = 8.0 Hz), 12.4; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –111.7 (dt, $^3J_{FHcis}$ = 20.8 Hz, $^3J_{FH}$ = 20.6 Hz, 1F); MS (ESI) *m/z* 451 $[M + H]^+$ (100), 329 (77), 195 (21), 105 (24), 91 (40); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{26}H_{28}FN_2O_4$ 451.2033, found 451.2047.

**(*Z*/*E*)-3-Benzoyl-1-[8-(benzyloxy)-2-fluorooct-2-en-1-yl]-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (30a).** General procedure C was followed with aminosulfone **6** (100 mg, 0.21 mmol, 1 equiv), 6-(benzyloxy)-hexanal (46 mg, 0.22 mmol, 1.05 equiv) and NaHMDS (1 M in THF, 0.32 mL, 0.32 mmol, 1.5 equiv) in THF (2 mL). The purification by flash chromatography (pentane/AcOEt, 65:35) afforded compound **30a** (60 mg, 61%) as a colorless oil (*E*/*Z* = 30:70). (*Z*)-**30a**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.92–7.90 (m, 2H), 7.65–7.62 (m, 1H), 7.50–7.46 (m, 2H), 7.35–7.26 (m, 5H), 7.13 (s, 1H), 4.97 (dt, $^3J_{HFtrans}$ = 36.3 Hz, $^3J_{HH}$ = 7.7 Hz, 1H), 4.49 (s, 2H), 4.37 (d, $^3J_{HF}$ = 17.5 Hz, 2H), 3.46 (t, $^3J_{HH}$ = 7.7 Hz, 2H), 2.14–2.13 (m, 2H), 1.96 (s, 3H), 1.63–1.60 (m, 2H), 1.40–1.39 (m, 4H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.8, 162.9, 152.1 (d, $^1J_{CF}$ = 253.7 Hz), 149.6, 139.0, 138.6, 135.0, 131.5, 130.4 (2C), 129.1 (2C), 128.3 (2C), 127.6 (2C), 127.5, 112.3 (d, $^2J_{CF}$ = 13.7 Hz), 111.1, 72.8, 70.2, 48.2 (d, $^2J_{CF}$ = 29.7 Hz), 29.4, 28.6, 25.7, 23.5 (d, $^3J_{CF}$ = 4.0 Hz), 12.4; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –118.2 (dt, $^3J_{FHtrans}$ = 36.3 Hz, $^3J_{FH}$ = 17.5 Hz, 1F); MS (ESI) *m/z* 465 $[M + H]^+$ (100), 343 (74), 217 (23), 195 (43), 105 (41), 91 (82); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{27}H_{30}FN_2O_4$ 465.2190, found 465.2207. (*E*)-**30a**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.93–7.90 (m, 2H), 7.65–7.61 (m, 1H), 7.50–7.46 (m, 2H), 7.36–7.27 (m, 5H), 7.13 (t, $^4J_{HH}$

= 1.1 Hz, 1H), 5.38 (dt, $^3J_{HFcis}$ = 21.0 Hz, $^3J_{HH}$ = 8.1 Hz, 1H), 4.49 (d, $^3J_{HF}$ = 20.4 Hz, 2H), 4.47 (s, 2H), 3.42 (t, $^3J_{HH}$ = 6.6 Hz, 2H), 2.11 (q, $^3J_{HH}$ = 6.6 Hz, 2H), 1.96 (d, $^4J_{HH}$ = 1.1 Hz, 3H), 1.58 (quint, $^3J_{HH}$ = 6.6 Hz, 2H), 1.38-1.34 (m, 4H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 168.8, 163.0, 152.4 (d, $^1J_{CF}$ = 245.7 Hz), 149.6, 139.4, 138.6, 135.0, 131.5, 130.5 (2C), 129.1 (2C), 128.3 (2C), 127.6 (2C), 127.5, 112.5 (d, $^2J_{CF}$ = 17.1 Hz), 111.0, 72.9, 70.1, 44.2 (d, $^2J_{CF}$ = 29.7 Hz), 29.4 (2C), 25.6, 25.1 (d, $^3J_{CF}$ = 8.0 Hz), 12.4; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –111.8 (dt, $^3J_{FHcis}$ = 21.0 Hz, $^3J_{FH}$ = 20.4 Hz, 1F); MS (ESI) *m/z* 465 $[M + H]^+$ (100), 343 (74), 217 (23), 195 (43), 105 (41), 91 (82); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{27}H_{30}FN_2O_4$ 465.2190, found 465.2207.

**(*Z*/*E*)-1-[6-(Benzyloxy)-2-fluorohex-2-en-1-yl]-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (28b).** General procedure E was followed with aminosulfone **6** (600 mg, 1.27 mmol, 1 equiv), 4-(benzyloxy)-butanal (237 mg, 1.33 mmol, 1.05 equiv) and NaHMDS (1 M in THF, 1.90 mL, 1.90 mmol, 1.5 equiv) in THF (13 mL). The crude mixture was treated with a solution of NaOH in MeOH (13 mL). The purification by flash chromatography (pentane/AcOEt, 1:1) afforded compound **28b** (249 mg, 59%) as a white solid (*E*/*Z* = 30:70). Mp 88 °C; (*Z*)-**28b**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 9.28 (sbr, 1H), 7.36–7.26 (m, 5H), 7.00 (s, 1H), 4.96 (dt, $^3J_{HFtrans}$ = 36.3 Hz, $^3J_{HH}$ = 7.3 Hz, 1H), 4.49 (s, 2H), 4.34 (d, $^3J_{HF}$ = 16.8 Hz, 2H), 3.47 (t, $^3J_{HH}$ = 7.3 Hz, 2H), 2.22 (q, $^3J_{HH}$ = 7.3 Hz, 2H), 1.91 (s, 3H), 1.70 (quint, $^3J_{HH}$ = 7.3 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 164.0, 152.6 (d, $^1J_{CF}$ = 253.6 Hz), 150.6, 139.2, 138.4, 128.3 (2C), 127.6 (2C), 127.5, 111.2 (d, $^2J_{CF}$ = 13.1 Hz), 111.1, 72.9, 69.4, 47.7 (d, $^2J_{CF}$ = 30.8 Hz), 28.9, 20.5 (d, $^3J_{CF}$ = 4.0 Hz), 12.3; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –117.6 (dt, $^3J_{FHtrans}$ = 36.3 Hz, $^3J_{FH}$ = 16.8 Hz, 1F); MS (ESI) *m/z* 333 $[M + H]^+$ (100); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{18}H_{22}FN_2O_3$ 333.1614, found 333.1612. (*E*)-**28b**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 9.59 (sbr, 1H), 7.36–7.26 (m, 5H), 7.01 (s, 1H), 5.35 (dt, $^3J_{HFcis}$ = 20.6 Hz, $^3J_{HH}$ = 7.5 Hz, 1H), 4.49 (s, 2H), 4.44 (d, $^3J_{HF}$ = 20.3 Hz, 2H), 3.50 (t, $^3J_{HH}$ = 7.5 Hz, 2H), 2.25 (q, $^3J_{HH}$ = 7.5 Hz, 2H), 1.90 (s, 3H), 1.72 (quint, $^3J_{HH}$ = 7.5 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 164.2, 152.9 (d, $^1J_{CF}$ = 246.3 Hz), 150.7, 139.5, 138.3, 128.3 (2C), 127.6 (2C), 127.5, 111.5 (d, $^2J_{CF}$ = 18.5 Hz), 110.9, 72.8, 68.9, 43.7 (d, $^2J_{CF}$ = 28.5 Hz), 29.4 (d, $^4J_{CF}$ = 2.1 Hz), 21.9 (d, $^3J_{CF}$ = 7.8 Hz), 12.3; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –111.4 (dt, $^3J_{FHcis}$ = 20.6 Hz, $^3J_{FH}$ = 20.3 Hz, 1F); MS (ESI) *m/z* 333 $[M + H]^+$ (100); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{18}H_{22}FN_2O_3$ 333.1614, found 333.1612.

**(*Z*/*E*)-1-[7-(Benzyloxy)-2-fluorohept-2-en-1-yl]-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (29b).** General procedure E was followed with aminosulfone **6** (600 mg, 1.27 mmol, 1 equiv), 5-(benzyloxy)-pentanal (255 mg, 1.33 mmol, 1.05 equiv) and NaHMDS (1 M

in THF, 1.90 mL, 1.90 mmol, 1.5 equiv) in THF (13 mL). The crude mixture was treated with a solution of NaOH in MeOH (13 mL). The purification by flash chromatography (pentane/AcOEt, 1:1) afforded compound **29b** (251 mg, 57%) as a white solid (*E*/*Z* = 27:73). Mp 89 °C; (*Z*)-**29b**: $^{1}$H NMR ($CDCl_3$, 400 MHz) $\delta$ 9.08 (sbr, 1H), 7.36–7.26 (m, 5H), 7.02 (s, 1H), 4.95 (dt, $^{3}J_{HFtrans}$ = 36.3 Hz, $^{3}J_{HH}$ = 7.5 Hz, 1H), 4.49 (s, 2H), 4.36 (d, $^{3}J_{HF}$ = 17.0 Hz, 2H), 3.47 (t, $^{3}J_{HH}$ = 7.5 Hz, 2H), 2.13 (q, $^{3}J_{HH}$ = 7.5 Hz, 2H), 1.92 (s, 3H), 1.62 (quint, $^{3}J_{HH}$ = 7.5 Hz, 2H), 1.47 (quint, $^{3}J_{HH}$ = 7.5 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 163.9, 152.5 (d, $^{1}J_{CF}$ = 253.4 Hz), 150.6, 139.3, 138.5, 128.3 (2C), 127.6 (2C), 127.5, 111.5 (d, $^{2}J_{CF}$ = 13.3 Hz), 111.1, 72.9, 69.9, 47.8 (d, $^{2}J_{CF}$ = 30.9 Hz), 29.2, 25.5, 23.4 (d, $^{3}J_{CF}$ = 3.8 Hz), 12.3; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –117.8 (dt, $^{3}J_{FHtrans}$ = 36.3 Hz, $^{3}J_{FH}$ = 17.0 Hz, 1F); MS (ESI) *m/z* 347 [M + H]$^{+}$ (100), 198 (12); HRMS (ESI) *m/z* [M + H]$^{+}$ calcd for $C_{19}H_{24}FN_2O_3$ 347.1771, found 347.1773. (*E*)-**29b**: $^{1}$H NMR ($CDCl_3$, 400 MHz) $\delta$ 8.97 (sbr, 1H), 7.36–7.26 (m, 5H), 7.01 (m, 1H), 5.35 (dt, $^{3}J_{HFcis}$ = 20.9 Hz, $^{3}J_{HH}$ = 7.6 Hz, 1H), 4.49 (s, 2H), 4.42 (d, $^{3}J_{HF}$ = 20.4 Hz, 2H), 3.48 (t, $^{3}J_{HH}$ = 7.6 Hz, 2H), 2.16 (q, $^{3}J_{HH}$ = 7.6 Hz, 2H), 1.91 (d, $^{4}J_{HH}$ = 0.9 Hz, 3H), 1.64 (quint, $^{3}J_{HH}$ = 7.6 Hz, 2H), 1.50 (quint, $^{3}J_{HH}$ = 7.6 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 164.0, 152.8 (d, $^{1}J_{CF}$ = 247.3 Hz), 150.5, 139.6, 138.5, 128.3 (2C), 127.6 (2C), 127.5, 112.1 (d, $^{2}J_{CF}$ = 17.6 Hz), 111.0, 72.9, 70.0, 43.8 (d, $^{2}J_{CF}$ = 28.7 Hz), 29.0, 26.4 (d, $^{4}J_{CF}$ = 2.1 Hz), 25.0 (d, $^{3}J_{CF}$ = 7.6 Hz), 12.3; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –111.5 (dt, $^{3}J_{FHcis}$ = 20.9 Hz, $^{3}J_{FH}$ = 20.4 Hz, 1F); MS (ESI) *m/z* 347 [M + H]$^{+}$ (100), 198 (12); HRMS (ESI) *m/z* [M + H]$^{+}$ calcd for $C_{19}H_{24}FN_2O_3$ 347.1771, found 347.1773.

**(*Z*/*E*)-1-[8-(Benzyloxy)-2-fluorooct-2-en-1-yl]-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (30b).** General procedure E was followed with aminosulfone **6** (600 mg, 1.27 mmol, 1 equiv), 6-(benzyloxy)-hexanal (274 mg, 1.33 mmol, 1.05 equiv) and NaHMDS (1 M in THF, 1.90 mL, 1.90 mmol, 1.5 equiv) in THF (13 mL). The crude mixture was treated with a solution of NaOH in MeOH (10 mL). The purification by flash chromatography (pentane/AcOEt, 1:1) afforded compound **30b** (288 mg, 63%) as a white solid (*E*/*Z* = 27:73). Mp 49 °C; $^{1}$H NMR ($CDCl_3$, 400 MHz) $\delta$ 9.83 (sbr, 2H, *E* and *Z*), 7.35–7.24 (m, 10H, *E* and *Z*), 7.01 (m, 2H, *E* and *Z*), 5.33 (dt, $^{3}J_{HFcis}$ = 20.9 Hz, $^{3}J_{HH}$ = 7.4 Hz, 1H, *E*), 4.93 (dt, $^{3}J_{HFtrans}$ = 36.6 Hz, $^{3}J_{HH}$ = 7.1 Hz, 1H, *Z*), 4.49 (s, 4H, *E* and *Z*), 4.43 (d, $^{3}J_{HF}$ = 20.4 Hz, 2H, *E*), 4.34 (d, $^{3}J_{HF}$ = 16.8 Hz, 2H, *Z*), 3.46 (t, $^{3}J_{HH}$ = 7.4 Hz, 2H, *E*), 3.45 (t, $^{3}J_{HH}$ = 7.1 Hz, 2H, *Z*), 2.16–2.06 (m, 4H, *E* and *Z*), 1.90 (m, 6H, *E* and *Z*), 1.62–1.58 (m, 4H, *E* and *Z*), 1.41–1.37 (m, 8H, *E* and *Z*); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 164.4 (*E*), 164.3 (*Z*), 152.6 (d, $^{1}J_{CF}$ = 246.8 Hz, *E*), 152.4 (d, $^{1}J_{CF}$ = 254.2 Hz, *Z*), 150.8 (*Z*), 150.7 (*E*), 139.5 (*E*), 139.2 (*Z*), 138.5 (2C, *E* and *Z*), 128.2 (s, 4C, *E* and *Z*), 127.5 (s, 4C, *E* and *Z*), 127.4 (2C, *E* and *Z*), 112.0 (d, $^{2}J_{CF}$ = 17.6 Hz,

*E*), 111.4 (d, $^2J_{CF}$ = 13.4 Hz, *Z*), 111.0 (*Z*), 110.8 (*E*), 72.7 (2C, *E* and *Z*), 70.1 (*Z*), 70.0 (*E*), 47.5 (d, $^2J_{CF}$ = 31.0 Hz, *Z*), 43.7 (d, $^2J_{CF}$ = 29.2 Hz, *E*), 29.3 (*E*), 29.3 (d, $^4J_{CF}$ = 2.7 Hz, *E*), 29.3 (*Z*), 28.6 (d, $^4J_{CF}$ = 1.3 Hz, *Z*), 25.6 (*Z*), 25.5 (*E*), 25.0 (d, $^3J_{CF}$ = 7.4 Hz, *E*), 23.4 (d, $^3J_{CF}$ = 3.7 Hz, *Z*), 12.2 (2C, *E* and *Z*); $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –111.6 (dt, $^3J_{FH\textit{cis}}$ = 20.9 Hz, $^3J_{FH}$ = 20.4 Hz, 1F, *E*), –118.0 (dt, $^3J_{FH\textit{trans}}$ = 36.6 Hz, $^3J_{FH}$ = 16.8 Hz, 1F, *Z*); MS (ESI) *m/z* 361 $[M + H]^+$ (100); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{20}H_{26}FN_2O_3$ 361.1927, found 361.1930.

**General procedure F: debenzylation in the preparation of fluorinated allylamines derived from thymine.** To a solution of fluoroalkene **28a-30a** (1 equiv), in $CH_2Cl_2$ (0.02 M) was added $TiCl_4$ (5 equiv) at 20 °C. After 16 h of stirring at 20 °C, a saturated aqueous solution of $NaHCO_3$ and then $Et_2O$ was added. After 30 min of stirring, the resulting mixture was filtered on celite. The filtrate was evaporated under reduced pressure to afford amino-alkenes **28c-30c**.

**(*Z*/*E*)-1-(2-Fluoro-6-hydroxyhex-2-en-1-yl)-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (28c).** General procedure F was followed with fluoroalkene **28b** (115 mg, 0.35 mmol, 1 equiv), $TiCl_4$ (0.19 mL, 1.73 mmol, 5 equiv) in $CH_2Cl_2$ (17 mL). The purification by flash chromatography ($CH_2Cl_2$/MeOH, 95:5) afforded compound **28c** (77 mg, 92%) as a colorless oil (*E*/*Z* = 25:75). (*Z*)-**28c**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 9.87 (sbr, 1H), 7.04 (s, 1H), 4.99 (dt, $^3J_{HF\textit{trans}}$ = 36.6 Hz, $^3J_{HH}$ = 7.5 Hz, 1H), 4.34 (d, $^3J_{HF}$ = 16.6 Hz, 2H), 3.61 (t, $^3J_{HH}$ = 7.3 Hz, 2H), 2.36 (s, 1H), 2.18 (q, $^3J_{HH}$ = 7.3 Hz, 2H), 1.90 (s, 3H), 1.63 (quint, $^3J_{HH}$ = 7.3 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 164.4, 152.6 (d, $^1J_{CF}$ = 253.6 Hz), 150.9, 139.5, 111.1, 110.9 (d, $^2J_{CF}$ = 13.1 Hz), 61.8, 47.9 (d, $^2J_{CF}$ = 30.2 Hz), 31.5 (d, $^4J_{CF}$ = 1.5 Hz), 20.0 (d, $^3J_{CF}$ = 4.0 Hz), 12.2; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –118.0 (dt, $^3J_{FH\textit{trans}}$ = 36.6 Hz, $^3J_{FH}$ = 16.6 Hz, 1F); MS (EI) *m/z* 243 $[M + H]^+$ (100), 168 (23), 127 (55); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{11}H_{16}FN_2O_3$ 243.1145, found 243.1141.

**(*Z*/*E*)-1-(2-Fluoro-7-hydroxyhept-2-en-1-yl)-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (29c).** General procedure F was followed with fluoroalkene **29b** (120 mg, 0.35 mmol, 1 equiv), $TiCl_4$ (0.19 mL, 1.73 mmol, 5 equiv) in $CH_2Cl_2$ (17 mL). The purification by flash chromatography ($CH_2Cl_2$/MeOH, 95:5) afforded compound **29c** (76 mg, 85%) as a colorless oil (*E*/*Z* = 20:80). $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 10.27 (sbr, 1H, *E*), 10.12 (sbr, 1H, *Z*), 7.05 (s, 1H, *E*), 7.04 (s, 1H, *Z*), 5.30 (dt, $^3J_{HF\textit{cis}}$ = 20.7 Hz, $^3J_{HH}$ = 8.2 Hz, 1H, *E*), 4.93 (dt, $^3J_{HF\textit{trans}}$ = 36.8 Hz, $^3J_{HH}$ = 7.6 Hz, 1H, *Z*), 4.44 (d, $^3J_{HF}$ = 20.7 Hz, 2H, *E*), 4.33 (d, $^3J_{HF}$ = 16.8 Hz, 2H, *Z*), 3.62 (t, $^3J_{HH}$ = 6.9 Hz, 2H, *E*), 3.59 (t, $^3J_{HH}$ = 6.9 Hz, 2H, *Z*), 2.75 (sbr, 1H, *E*), 2.67 (sbr, 1H, *Z*), 2.13 (q, $^3J_{HH}$ = 6.9 Hz, 2H, *E*), 2.09 (q, $^3J_{HH}$ = 6.9 Hz, 2H, *Z*), 1.88 (s, 6H, *E* and *Z*), 1.57–

1.49 (m, 4H, *E* and *Z*), 1.45–1.37 (m, 4H, *E* and *Z*); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 164.5 (*E*), 164.4 (*Z*), 152.7 (d, $^1J_{CF}$ = 246.0 Hz, *E*), 152.5 (d, $^1J_{CF}$ = 253.5 Hz, *Z*), 151.1 (*E*), 151.0 (*Z*), 139.9 (*E*), 139.5 (*Z*), 111.9 (d, $^2J_{CF}$ = 18.1 Hz, *E*), 111.3 (d, $^2J_{CF}$ = 13.6 Hz, *Z*), 111.1 (2C, *E* and *Z*), 62.1 (*Z*), 61.7 (*E*), 47.8 (d, $^2J_{CF}$ = 30.9 Hz, *Z*), 44.0 (d, $^2J_{CF}$ = 28.7 Hz, *E*), 31.9 (*Z*), 31.6 (*E*), 25.7 (d, $^4J_{CF}$ = 2.2 Hz, *E*), 24.9 (d, $^4J_{CF}$ = 1.5 Hz, *Z*), 24.7 (d, $^3J_{CF}$ = 8.0 Hz, *E*), 23.2 (d, $^3J_{CF}$ = 4.0 Hz, *Z*), 12.2 (2C, *E* and *Z*); $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –111.8 (dt, $^3J_{FH\textit{cis}}$ = 20.7 Hz, $^3J_{FH}$ = 20.7 Hz, 1F, *E*), –118.2 (dt, $^3J_{FH\textit{trans}}$ = 36.8 Hz, $^3J_{FH}$ = 16.8 Hz, 1F, *Z*); MS (EI) *m/z* 297 $[M + H]^+$ (51), 127 (100); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{12}H_{18}FN_2O_3$ 257.1301, found 257.1306.

**(*Z*/*E*)-1-(2-Fluoro-8-hydroxyoct-2-en-1-yl)-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (30c).** General procedure F was followed with fluoroalkene **30b** (70 mg, 0.19 mmol, 1 equiv), $TiCl_4$ (0.11 mL, 0.97 mmol, 5 equiv) in $CH_2Cl_2$ (10 mL). The purification by flash chromatography ($CH_2Cl_2$/MeOH, 95:5) afforded compound **30c** (51 mg, 97%) as a colorless oil (*E*/*Z* = 21:79). $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 9.87–9.71 (m, 2H, *E* and *Z*), 7.05 (s, 1H, *E*), 7.03 (s, 1H, *Z*), 5.32 (dt, $^3J_{HF\textit{cis}}$ = 20.9 Hz, $^3J_{HH}$ = 7.8 Hz, 1H, *E*), 4.94 (dt, $^3J_{HF\textit{trans}}$ = 36.5 Hz, $^3J_{HH}$ = 7.8 Hz, 1H, *Z*), 4.45 (d, $^3J_{HF}$ = 20.4 Hz, 2H, *E*), 4.34 (d, $^3J_{HF}$ = 16.8 Hz, 2H, *Z*), 3.61 (t, $^3J_{HH}$ = 6.4 Hz, 4H, *E* and *Z*), 2.21–2.09 (m, 6H, *E* and *Z*), 1.90 (s, 6H, *E* and *Z*), 1.57–1.52 (m, 4H, *E* and *Z*), 1.38–1.36 (m, 8H, *E* and *Z*); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 164.4 (2C, *E* and *Z*), 152.7 (d, $^1J_{CF}$ = 246.6 Hz, *E*), 152.4 (d, $^1J_{CF}$ = 253.7 Hz, *Z*), 151.0 (*E*), 150.9 (*Z*), 139.7 (*E*), 139.4 (*Z*), 112.1 (d, $^2J_{CF}$ = 17.7 Hz, *E*), 111.5 (d, $^2J_{CF}$ = 13.1 Hz, *Z*), 111.1 (*Z*), 111.0 (*E*), 62.5 (*Z*), 62.4 (*E*), 47.8 (d, $^2J_{CF}$ = 30.4 Hz, *Z*), 44.9 (d, $^2J_{CF}$ = 28.7 Hz, *E*), 32.2 (*Z*), 32.1 (*E*), 29.2 (d, $^4J_{CF}$ = 2.1 Hz, *E*), 28.5 (d, $^4J_{CF}$ = 1.3 Hz, *Z*), 25.1 (2C, *E* and *Z*), 25.0 (d, $^3J_{CF}$ = 4.4 Hz, *E*), 23.4 (d, $^3J_{CF}$ = 3.8 Hz, *Z*), 12.3 (2C, *E* and *Z*); $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ –111.6 (dt, $^3J_{FH\textit{cis}}$ = 20.9 Hz, $^3J_{FH}$ = 20.4 Hz, 1F, *E*), –118.2 (dt, $^3J_{FH\textit{trans}}$ = 36.5 Hz, $^3J_{FH}$ = 16.8 Hz, 1F, *Z*); MS (ESI) *m/z* 271 $[M + H]^+$ (100), 253 (17), 127 (20); HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{13}H_{20}FN_2O_3$ 271.1458, found 271.1458.

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## ASSOCIATED CONTENT

**Supporting Information**

NMR spectra for compounds **2, II, 3–16**, **17a,b–25a,b**, **26**, **27**, **28a,b,c–30a,b,c**. This material is free of charge via the internet at http://pubs.acs.org.

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