Facile perfluoroalkylation of uracils and uridines at the C-5 position

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Abstract

Perfluoroalkylation at the C-5 position of uracil has been achieved in yields of 38–56% by the reaction of its bis(trimethylsilyl) derivative with bis(perfluoroalkanoyl) peroxides and the hydrolytic deprotection of the silylated products. A substituent or nitrogen replacement at C-6 does not interfere with perfluoroalkylation at C-5, but no significant reaction occurs at C-6 when C-5 is blocked.

Introduction

The impressive antimetabolic activities of 5-(trifluoromethyl)uracil (**5a**) and its furanosides [1] have stimulated research into improved methods of synthesis, as well as methods which may provide higher perfluoroalkyl homologs. We have been interested in improving accessibility to these higher homologs, both for the sake of examining their own biological activities and for their use as precursors to even less accessible functionalities at C-5 [2]. In the presence of copper bronze in DMSO, perfluoroalkyl iodides have been found to perfluoroalkylate uracil, uridine and their derivatives in yields rarely exceeding 3–6% [3]. Although 5-iodouracil proved to be unreactive toward replacement of iodine in this work, Lin and Gao [4] succeeded in obtaining the perfluoroethyl derivative of a protected uridine in 17% yield from the 5-iodo compound. Photochemical perfluoroalkylation of the same pyrimidines with bis(perfluoroalkyl)mercury has also been explored [5]: while yields were significantly better in favorable cases, the results were inconsistent. Furthermore, the cost and toxicity of the reagent may limit the appeal of the latter method.

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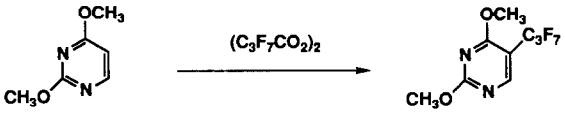
Results and discussion

The perfluoroalkylation of electron-rich heterocycles with bis(perfluoroalkanoyl) peroxides has been described previously, the expected products being obtained in moderately high yields [6]. Our application of this method to uracil failed (low solubility of uracil in Freon-113). We then investigated the reactivity of 2,4-dimethoxypyrimidine (**1**), which we anticipated to be more soluble and more reactive toward an electrophilic perfluoroalkyl radical by virtue of its electron-releasing methoxy groups. Reaction of **1** with bis(heptafluorobutyryl) peroxide gave the 5-heptafluoropropyl derivative **2** in 47% yield (Table 1). In contrast, compound **1** failed to react with perfluorohexyllithium [7]. Encouraged by this first result, we turned to pyrimidine derivatives from which the uracil might be more easily regenerated than from the dimethoxy derivative [7].



1 **2**

2,4-Bis(trimethylsilyloxy)pyrimidine (**3**) was prepared by reaction of uracil with chlorotrimethylsilane and triethylamine in dioxan [8]. Reaction of the

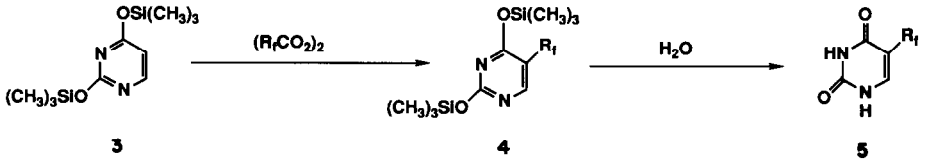
TABLE 1

Reactions of protected pyrimidines with bis(perfluoroalkanoyl) peroxides

Compound	$(R_fCO_2)_2$[a]		Product	Yield[b] (%)
	R_f	Equiv.		
Uracil	C_3F_7	0.5	no reaction	
1	C_3F_7	0.5	**2**	46.9
3	CF_3	0.5	**5a**	12.7
3	C_3F_7	0.5	**5b**	56.5
3	C_3F_7	0.75	**5b**	50.0
3	C_3F_7	1.2	**5b**	42.8[c]
3	C_6F_{13}	0.5	**5c**	37.7
12a[d]	C_3F_7	1.0	**12b**	36.1
13a[d]	C_3F_7	1.0	**13b**	41.0
14a[d]	C_3F_7	1.0	**14b**	19.7
15a[d]	C_3F_7	1.0	**15b**[e]	12.9

[a]For reaction conditions, see Experimental section.
[b]Isolated yield based on peroxide.
[c]Isolated yield based on pyrimidine.
[d]As trimethylsilyl derivative (not isolated).
[e]A second product, obtained in comparable yield, is still under investigation.

moisture-sensitive **3** with bis(perfluorobutyryl) peroxide gave a mixture which, according to GC/MS analysis, contained the expected product, **4b**, which was hydrolyzed to the uracil derivative **5b** prior to purification. The reaction conditions and the yields for several runs are given in Table 1.



At least for the preparation of the perfluoropropyl derivative **5b**, the optimum yield was realized by the use of 0.5 equiv. of the peroxide. Structural assignment is based on the correspondence of the ^{1}H NMR signal for the residual ring CH with that of H-6 (δ 8.01 ppm) in the authentic 5-(trifluoromethyl)uracil (**5a**). In no case did the crude product give evidence for the formation of the isomeric 6-(perfluoroalkyl)uracil (H-5, δ 5.95 ppm [7]) or for perfluoroalkylation on nitrogen or oxygen. In a similar manner, **5c** was obtained in 38% yield. Preparation of the known **5a** by our method proved more difficult in that a sealed tube was required to achieve a higher reaction temperature (70 °C) and yields were lower than those for **5b** or **5c**.

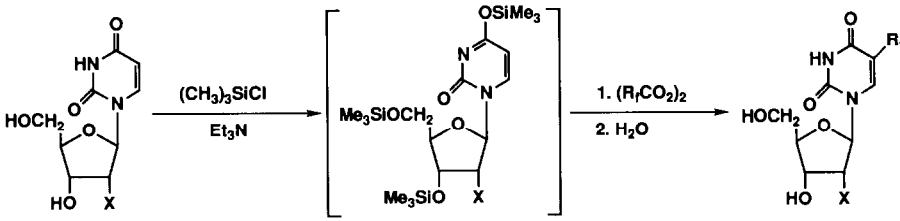
Analogous reactions with uridine (**6**), 2′-deoxyuridine (**7**), or their sugar-acetylated derivatives, failed; nor did silylation of the pyrimidine ring in the sugar-acetylated derivatives lead to the expected products. After *both* the sugar and pyrimidine moieties had been converted to their silyl derivatives (**8**, **9**) [9], however, reaction did occur and the desired 5-perfluoroalkyl derivatives **10** and **11** were obtained in yields of 26–42% (Table 2). Presumably, the success of the latter route is due to the combination of increased solubility and increased electron density in the pyrimidine ring.

TABLE 2

Reactions of persilylated uridines with bis(perfluoroalkanoyl) peroxides[a]

Compound	$(R_fCO_2)_2$		Product	Yield[b] (%)
	R_f	Equiv.		
8	C_3F_7	1.2	**10b**	38.6
8	C_6F_{13}	1.2	**10c**	37.6
9	C_3F_7	1.2	**11b**	26.0
9	C_6F_{13}	1.2	**11c**	41.9

[a]All reactions conducted for 20 h at 30 °C in Freon-113 as solvent.
[b]Isolated yield based on pyrimidine.



6, X = OH **8**, X = $OSiMe_3$ **10**, X = OH

7, X = H **9**, X = H **11**, X = H

a, $R_f = CF_3$; b, $R_f = C_3F_7$; c, $R_f = C_6F_{13}$;

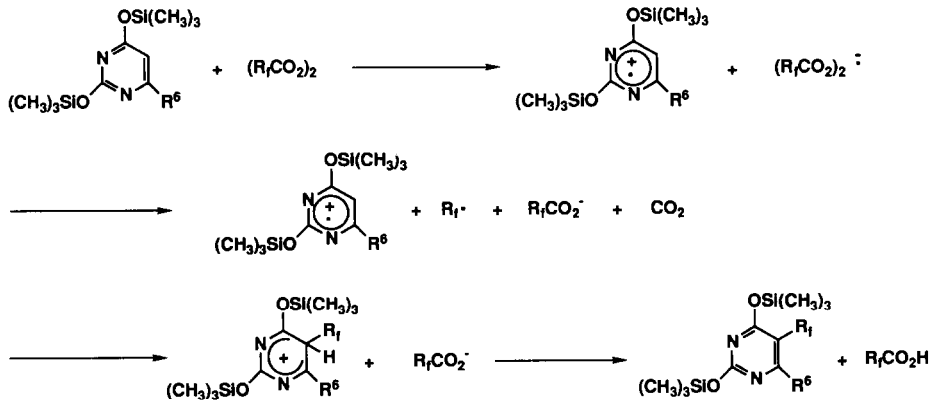
Substitution at the 6-position of uracil does not interfere with perfluoroalkylation at C-5 via the silylated compound. Thus, 6-methyluracil (**12a**) gave the 5-heptafluoropropyl derivative **12b** in 36% yield and 6-(trifluoromethyl)uracil (**13a**) gave **13b** in 41% yield (Table 1). On the other hand, substitution at C-5 failed to direct perfluoroalkylation to C-6 to any significant extent. Thus, reaction of the bis(trimethylsilyl) derivative of thymine with bis(heptafluorobutyryl) peroxide gave only 3% of a crude product whose MS and ^{19}F NMR spectra were consistent with expectations for 6-(heptafluoropropyl)thymine, but further purification could not be achieved. Somewhat low yields were obtained with 2-thiouracil (**14b**, 20% yield) and with 6-azauracil (**15b**, 13%). In the latter case, further elution of silica gel provided an additional product in comparable yield whose structure is under investigation.

12 **13**

14 **15**

a, R = H; b, R = C_3F_7;

The silylated derivative of 2-hydroxypyrimidine failed to undergo perfluoroalkylation. Results with cytosine were also unrewarding. Direct reaction of unprotected cytosine gave 13% of the N^4-heptafluorobutyryl derivative. Silylation of cytosine with chlorotrimethylsilane was incomplete; the bis(trimethylsilyl) derivative was obtained by the use of the more powerful reagent *N*,*O*-bis(trimethylsilyl)trifluoroacetamide, but no perfluoroalkylation



Scheme 1.

was achieved. Similarly, the more stable trimethylsilyl derivative of N^4-acetylcytosine failed to give a product.

The single electron transfer (SET) mechanism has been proposed for the perfluoroalkylation of electron-rich heterocyclic compounds [6]. Although the pyrimidine ring is electron deficient, the introduction of trimethylsilyloxy groups increases the level of the HOMO; the ring is now sufficiently electron-rich to participate in the SET mechanism (Scheme 1). The trimethylsilyloxy groups not only facilitate the formation of the cation radical by electron donation but also stabilize the carbocation resulting from perfluoroalkyl addition. Thus, the substrates containing two trimethylsilyloxy groups provide ring-perfluoroalkylated compounds in moderate yield. Although the silylation of cytosines also increases the HOMO level, perfluoroalkylation by the SET mechanism does not occur, not only because the N—TMS bond of the silylated substrate is less stable than the O—TMS bond, but also because the intermediates readily release the hydrogen of the amino group. The attack of a perfluoroalkyl radical at C-6 would lead to an intermediate cation which cannot be stabilized by delocalization with silyloxy group. We have not determined whether **14a** leads to a mono- or bis-silyloxy derivative, but even a bis-derivative should be less reactive since sulfur is less effective than oxygen in stabilizing a carbocation by delocalization. The yield in perfluoroalkylation of **15a** is reduced because of side-reactions involving the nitrogen at C-6. The silylated derivatives of sugar-acetylated uridine are barely soluble in Freon and provided no perfluoroalkylated compounds. Evidently, solubility of the substrate is a critical factor in electron transfer and/or addition of the perfluoroalkyl radical.

Experimental

General methods

Melting and boiling points are uncorrected. ^{1}H NMR spectra were recorded on a Hitachi R-90H spectrometer at 90 MHz, with tetramethylsilane as internal

reference and DMSO-d_6 as solvent. ^{19}F NMR spectra were recorded on a Hitachi R-90F spectrometer at 84.68 MHz with DMSO-d_6 as solvent; positive δ values are downfield from the external reference, trifluoroacetic acid. Mass spectral data were obtained on a Hitachi M-80 spectrometer by electron-impact ionization at 70 eV (unless otherwise indicated). IR spectra (in KBr) were obtained with a JASCO IR-810 spectrometer. All bis(perfluoroalkanoyl) peroxides were supplied by Nippon Oil & Fats Co. Ltd. Other reagents were obtained from commercial sources and were used without further purification. Elemental analyses for all products are summarized in Table 3.

Method A. Preparation of 5-perfluoroalkyl derivatives of uracil

To a solution of 1.28 g (5 mmol) of 2,4-bis(trimethylsilyloxy)pyrimidine (**3**) [8] in 20 ml of Freon-113 (ClF_2CCCl_2F) was added, over 1 min at ambient temperature, 21.6 g of a 5.0% solution of bis(heptafluorobutyryl) peroxide in Freon-113 (2.5 mmol). The reaction mixture was stirred at 30 °C for 3 h and heated at reflux (48 °C) for 2 h. The mixture was cooled to ambient temperature, 100 ml of water was added and the two-phase system was stirred for 2 h. The mixture was extracted with three portions of ethyl acetate (150, 100 and 100 ml), the combined extracts were washed with saturated $NaHCO_3$ solution and with water, dried (Na_2SO_4) and evaporated. Silica gel chromatography of the colorless residue (eluent, ethyl acetate) gave 0.40 g (56.5%) of 5-(heptafluoropropyl)uracil (**5b**). The yields in several runs are given in Table 1.

2,4-Dimethoxy-5-(heptafluoropropyl)pyrimidine (**2**) (nc): B.p. 214–215 °C. IR (cm^{-1}): 1340 (CF_3); 1235 (CF_2). ^1H NMR δ: 4.05 (s, 3H, OCH_3); 4.08 (s, 3H, OCH_3); 7.99 (s, 1H, H-6) ppm. ^{19}F NMR δ: −3.31 (t, 3F, J=9.93 Hz, γ-CF_3); −32.64 (q, 2F, J=9.92 Hz, α-CF_2) −48.93 (s, 2F, β-CF_2)* ppm. MS (*m/z*): 308 (M^+, 8.1); 278 (5.7); 189 (100).

5-(Heptafluoropropyl)uracil (**5b**) (nc): M.p. 258–259 °C dec. (EtOAc). IR (cm^{-1}): 3160 (NH); 1680; 1750 (C=O); 1360 (CF_3); 1230 (CF_2). ^1H NMR δ: 7.99 (s, H-6) ppm. ^{19}F NMR δ: −1.52 (t, 3F, J=8.68 Hz, γ-CF_3); −30.67 (q, 2F, J=9.93 Hz, α-CF_2); −46.87 (s, 2F, β-CF_2) ppm. MS (*m/z*): 280 (M^+, 5.0); 261 (1.3); 161 (100).

5-(Tridecafluorohexyl)uracil (**5c**): Eluent, ethyl acetate; m.p. 277–278 °C dec. (EtOAc) (250 °C dec. [3a]). IR (cm^{-1}): 3240 (NH); 1670; 1760 (C=O); 1325 (CF_3); 1255 (CF_2). ^1H NMR δ: 7.98 (s, H-6) ppm. ^{19}F NMR δ: −2.08 (t, 3F, J=8.7 Hz, ζ-CF_3); −29.94 (t, 2F, J=13.7 Hz, α-CF_2); −42.60 (br s, 2F, β-CF_2); −43.39 (br s, 2F, γ-CF_2); −44.21 (br s, 2F, δ-CF_2); −47.53 (br s, 2F, J=7.4 Hz, ϵ-CF_2) ppm. MS (*m/z*): 430 (M^+, 4.6); 411 (2.7); 161 (100).

The low solubility of **4c** in both ethyl acetate and water retarded complete hydrolysis; product **5c** was contaminated with trace amounts of impurities which were apparently generated during chromatography.

*The magnitudes of the F–F couplings in the perfluoroalkyl chains are consistent with the observations that four-bond coupling is considerably stronger than three-bond coupling [10].

TABLE 3

Analytical data for perfluoroalkyluracils and uridines

Compound	Empirical formula	Molecular weight	Calc. (%)			Found (%)		
			C	H	N	C	H	N
2	$C_9H_7F_7N_2O_2$	308.17	35.08	2.29	9.09	34.94	2.29	9.04
5b	$C_7H_3F_7N_2O_2$	280.11	30.02	1.08	10.00	30.09	1.10	10.01
5c	$C_{10}H_3F_{13}N_2O_2$	430.15	27.92	0.70	6.51	27.87	0.73	6.51
10b	$C_{12}H_{11}F_7N_2O_6$	412.23	34.96	2.69	6.80	35.00	2.73	6.74
10c	$C_{15}H_{11}F_{13}N_2O_6$	562.26	32.04	1.97	4.98	32.13	1.99	4.96
11b	$C_{12}H_{11}F_7N_2O_5$[a]	418.26	37.33	3.13	6.70	37.35	3.14	6.49
11c	$C_{15}H_{11}F_{13}N_2O_5$	546.26	32.98	2.03	5.13	33.08	2.04	5.08
12b	$C_8H_5F_7N_2O_2$	294.14	32.67	1.71	9.53	32.74	1.75	9.49
13b	$C_8H_2F_{10}N_2O_2 \cdot H_2O$	366.13	26.25	1.10	7.65	26.20	1.10	7.75
14b	$C_7H_3F_7N_2OS$[a]	318.20	30.20	1.58	8.80	30.13	1.53	8.81
15b	$C_6H_2F_7N_3O_2$	281.10	25.64	0.72	14.95	25.79	0.76	15.02

[a]Calculated percentage values include 0.25EtOAc; the solvent was not lost at 80 °C *in vacuo* (24 h).

*Preparation of 5-(trifluoromethyl)uracil (**5a**)*

A solution of 1.55 g (6 mmol) of **3** in 30 ml of Freon-113 was placed in a large ampoule. While an argon atmosphere was maintained, 113.5 g of a solution (0.6%) of bis(trifluoroacetyl) peroxide in Freon-113 (3 mmol) was added dropwise. The ampoule was sealed under vacuum and maintained at 70 °C for 5 h, since bis(trifluoroacetyl) peroxide is more stable than its higher homologs and requires a higher reaction temperature for fragmentation. The contents of the ampoule were evaporated, 100 ml of water was added to the residue and the mixture was heated at reflux for 1 h. The mixture was concentrated to dryness and the residue was extracted with ethyl acetate (4×100 ml). The combined extracts were evaporated and the residual material was subjected to silica gel chromatography. The product obtained by elution with ethyl acetate/2-propanol/water, 75:16:9, was impure. A cleaner product (0.069 g, 12.7%) was obtained by elution with ethyl acetate alone, but the low solubility of **5a** in ethyl acetate required the use of relatively large volumes of the eluting solvent.

Compound **5a**: M.p. 236–237 °C dec. (EtOAc) (247 °C [5a]; 238–241 °C [5b]). IR (cm^{-1}): 3240 (NH); 1680; 1715; 1750 (C=O); 1350 (CF_3). ^1H NMR δ: 8.01 (s, H-6) ppm. ^{19}F NMR δ: 16.90 (s) ppm. MS (*m/z*): 180 (M^+, 100); 137 (44).

Method B. 5-Perfluoroalkyl derivatives of 6-substituted uracils and uracil analogs

A stirred suspension of 6-methyluracil (**12a**, 0.76 g, 6.03 mmol) in 30 ml of dry dioxan containing 1.83 g (18.1 mmol) of triethylamine was maintained under argon at ambient temperature while 1.96 g (18.0 mmol) of chlorotrimethylsilane was added dropwise. The immediate formation of a white precipitate was accompanied by a slight rise in temperature. The reaction mixture was stirred for 15 h, the precipitate was removed by filtration and volatile materials were removed by evaporation under vacuum. To the residual pale yellow oil was added 30 ml of Freon-113 to give a white suspension. To the mixture was added 51.37 g of a 5.0% solution of bis(heptafluorobutyryl) peroxide in Freon-113 (6.03 mmol). The reaction mixture was stirred for 2 h at 30 °C and then heated at reflux for 1.5 h. Following removal of the solvent under reduced pressure, the residual dark yellow oil was hydrolyzed by addition of water (100 ml) and ethyl acetate (100 ml) and stirring for 2 h. The aqueous layer was neutralized with saturated $NaHCO_3$ solution and extracted with ethyl acetate (4×100 ml). The combined extracts were dried (Na_2SO_4) and evaporated to give a light yellow powder. Silica gel chromatography with ethyl acetate gave **12b** (0.64 g, 36.1%). Yields are given in Table 1.

5-(Heptafluoropropyl)-6-methyluracil (**12b**) (nc): Eluent, ethyl acetate; m.p. 274–277 °C dec. (EtOAc). IR (cm^{-1}): 3150 (NH); 1690; 1760 (C=O); 1360 (CF_3); 1230 (CF_2). ^1H NMR δ: 2.23 (t, J=3.5 Hz, CH_3); 11.46 (br s, NH) ppm. ^{19}F NMR δ: −1.41 (t, 3F, J=8.7 Hz, γ-CF_3); −24.90 (m, 2F,

α-CF_2); −46.90 (s, 2F, β-CF_2) ppm. MS (*m/z*): 294 (M^+, 24); 275 (9); 175 (100).

5-(Heptafluoropropyl)-6-(trifluoromethyl)uracil (**13b**) (nc): Eluent, ethyl acetate followed by methanol/ethyl acetate 1:9; m.p. 162–165 °C dec. (EtOAc). IR (cm^{-1}): 3160 (NH); 1650 (C=O); 1350; 1370 (CF_3); 1240 (CF_2). ^1H NMR δ: 10.40 (br s, NH) ppm. ^{19}F NMR δ: 14.88 (m, 3F, 6-CF_3); −1.55 (t, 3F, J=9.9 Hz, γ-CF_3); −22.50 (m, 2F, α-CF_2); −43.68 (q, 2F, J=9.9 Hz, β-CF_2) ppm. MS (*m/z*): 348 (M^+, 16); 329 (12); 286 (25); 236 (55); 229 (100); 186 (100).

5-(Heptafluoropropyl)-2-thiouracil (**14b**) (nc): Eluent, ethyl acetate; m.p. 249–251 °C dec. (EtOAc). IR (cm^{-1}): 3090 (NH); 1690 (C=O); 1360 (CF_3); 1240 (CF_2); 1210 (C=S). ^1H NMR δ: 7.88 (s, H-6) ppm. ^{19}F NMR δ: −1.38 (t, 3F, J=9.9 Hz, γ-CF_3); −31.55 (q, 2F, J=9.9 Hz, α-CF_2); −46.76 (s, 2F, β-CF_2) ppm. MS (*m/z*): 296 (M^+, 100); 238 (10); 191 (19); 177 (45).

5-(Heptafluoropropyl)-6-azauracil (**15b**) (nc): Eluent, ethyl ether followed by ethyl acetate; m.p. 158–161 °C dec. (EtOAc). IR (cm^{-1}): 3250 (NH); 1710; 1750 (C=O); 1360 (CF_3); 1240 (CF_2). ^1H NMR δ: 12.4 (br s, NH); 13.2 (br s, NH) ppm. ^{19}F NMR δ: −1.26 (t, 3F, J=8.7 Hz, γ-CF_3); −34.16 (q, 2F, J=8.7 Hz, α-CF_2); −46.67 (s, 2F, β-CF_2) ppm. MS (*m/z*): 281 (M^+, 29); 262 (13); 210 (44); 162 (100).

Method C. Perfluoroalkylation of pyrimidine nucleosides

Method B was followed, except that 5 equiv. of chlorotrimethylsilane and of triethylamine were used to prepare the persilylated intermediate. The perfluoroalkylation mixture, containing 1.2 equiv. of the bis(perfluoroalkanoyl) peroxide, was kept at 30 °C for 20 h. Yields are given in Table 2.

5-(Heptafluoropropyl)uridine (**10b**) (nc): Eluent, ethyl acetate; m.p. 207–209 °C dec. (EtOAc). IR (cm^{-1}): 3340 (OH); 1680; 1710 (C=O); 1360 (CF_3); 1240 (CF_2). ^1H NMR δ: 3.67 (br s, 2H, CH_2); 3.80–4.20 (3H, OHs); 5.00–5.60 (3H, H-2′, 3′, 4′); 5.76 (d, 1H, H-1′); 8.85 (s, 1H, H-6); 11.81 (br s, 1H, NH) ppm. ^{19}F NMR δ: −1.35 (t, 3F, J=8.7 Hz, γ-CF_3); −30.34 (q, 2F, J=8.7 Hz, α-CF_2); −46.87 (s, 2F, β-CF_2)ppm. MS (EI, 20 eV) (*m/z*): 394 ($M^+ - H_2O$, 8.5); 339 (7.1); 281 (25); MS (CI, isobutane, 20 eV) (*m/z*): 413 ($M^+ + 1$).

5-(Tridecafluorohexyl)uridine (**10c**): Eluent, ethyl acetate; m.p. 214–216 °C dec. (EtOAc) (220–223 °C [3a]). IR (cm^{-1}): 3400 (OH); 1695; 1740 (C=O); 1370 (CF_3); 1240 (CF_2). ^1H NMR δ: 3.68 (br s, 2H, CH_2); 3.80–4.20 (3H, OHs); 5.00–5.65 (3H, H-2′, 3′, 4′); 5.77 (d, 1H, H-1′); 8.68 (s, 1H, H-6); 11.81 (br s, 1H, NH) ppm. ^{19}F NMR δ: −1.93 (t, 3F, J=8.7 Hz, ζ-CF_3); −29.56 (t, 2F, J=8.7 Hz, α-CF_2); −42.54 (br s, 2F, β-CF_2); −43.27 (br s, 2F, γ-CF_2); −44.07 (br s, 2F, δ-CF_2); −47.37 (br s, 2F, ϵ-CF_2) ppm. MS (EI, 20 eV) (*m/z*): 544 ($M^+ - H_2O$, 6.3); 489 (5.5); 431 (21); MS (CI, isobutane, 20 eV) (*m/z*): 563 ($M^+ + 1$).

5-(Heptafluoropropyl)-2′-deoxyuridine (**11b**) (nc): Eluent, ethyl acetate; m.p. 158–159 °C dec. (EtOAc). IR (cm^{-1}): 3450 (OH); 1690; 1740 (C=O); 1350 (CF_3); 1240 (CF_2). ^1H NMR δ: 1.95–2.60 (m, 2H, H-2′); 3.40–3.60

(br s, 2H, H-5′); 3.60–4.00 (br s, 1H, H-4′); 4.70–5.00 (m, 1H, H-3′); 4.50–5.60 (m, 2H, OHs); 6.12 (t, 1H, $J=6.05$ Hz, H-1′); 8.85 (s, 1H, H-6); 11.81 (br s, 1H, NH) ppm. ^{19}F NMR δ: −1.38 (t, 3F, $J=8.7$ Hz, γ-CF_3); −30.47 (q, 2F, $J=9.9$ Hz, α-CF_2); −46.93 (s, 2F, β-CF_2) ppm. MS (EI, 20 eV) (*m/z*): 336 (10); 307 (19); 304 (20); MS (CI, isobutane, 20 eV) (*m/z*): 397 ($M^+ + 1$).

5-(Tridecafluorohexyl)-2′-deoxyuridine (**11c**) (nc): Eluent, ethyl acetate; m.p. 183–185 °C dec. (EtOAc). IR (cm^{-1}): 3450 (OH); 1680; 1740 (C=O); 1370 (CF_3); 1240 (CF_2). ^{1}H NMR δ: 1.95–2.60 (m, 2H, H-2′); 3.50–3.80 (br s, 2H, H-5′); 3.80–4.00 (br s, 1H, H-4′); 4.20–4.45 (m, 1H, H-3′); 5.00–5.50 (m, 2H, OHs); 6.13 (t, 1H, $J=5.93$ Hz, H-1′); 8.85 (s, 1H, H-6) ppm. ^{19}F NMR δ: −1.82 (br s, 3F, ζ-CF_3); −29.65 (t, 2F, $J=12.4$ Hz, α-CF_2); −42.53 (br s, 2F, β-CF_2); −43.18 (br s, 2F, γ-CF_2); −44.00 (br s, 2F, δ-CF_2); −47.31 (br s, 2F, ϵ-CF_2) ppm. MS (EI, 20 eV) (*m/z*): 457 (6.7); 454 (6.1); 431 (17); MS (CI, isobutane, 20 eV) (*m/z*): 547 ($M^+ + 1$).

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