Synthesis of Fluorinated Homo-*C*-Nucleoside Analogues from New Carbohydrate-Derived Acylsilanes

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Abstract: The stereocontrolled synthesis of new carbohydrate-derived acylsilanes with the silylcarbonyl moiety linked to the anomeric carbon via a methylene group is described. Reaction of these acylsilanes with perfluoroorganometallic reagents followed by treatment with hydrazines or amidines led to new polyfluorinated homo-*C*-nucleoside analogues, in a one-pot or two-step transformation, respectively.

Key words: acylsilane, carbohydrate, heterocycles, organofluorine, *C*-nucleoside

The chemistry of *C*-nucleosides[1] has received recently considerable attention due to the biological activities of naturally occurring compounds such as showdomycin, formycin or oxazomycin.[2] Homo-*C*-nucleosides are a growing class of nucleosides[3] which are structurally composed of a sugar portion and an aglycon linked via a methylene bridge between the anomeric carbon atom and a carbon atom in the aglycon. The incorporation of one or several fluorine atoms in biologically active molecules has been shown to be of advantage both for improved activity and higher bioavailability.[4] Previous papers in this series have demonstrated the versatility of the reaction of perfluoro organometallic reagents with acylsilanes, leading to 1-(trialkylsilyl)perfluoroalkyl carbinols, 1-alkyl-1-(trialkylsilyloxy)perfluoroalk-1-enes or the corresponding hemifluorinated enones.[5] Treatment of these compounds with bis(nucleophiles) gave various nitrogen-containing heterocycles such as imidazolidines/oxazolidines and diazepines/thiazepines,[6] pyrazoles[7] and pyrimidines.[8] The synthesis of such heterocycles linked to a carbohydrate moiety was also exemplified from carbohydrate-derived acylsilanes.[7,8]

In order to form fluorinated homo-*C*-nucleoside analogues, we performed the synthesis of new compounds bearing an acylsilane function linked to the anomeric carbon atom via a methylene group. This paper is devoted to the account of this synthetic work and to the application of these new carbohydrate derived acylsilanes to the synthesis of fluorinated homo-*C*-nucleoside analogues.

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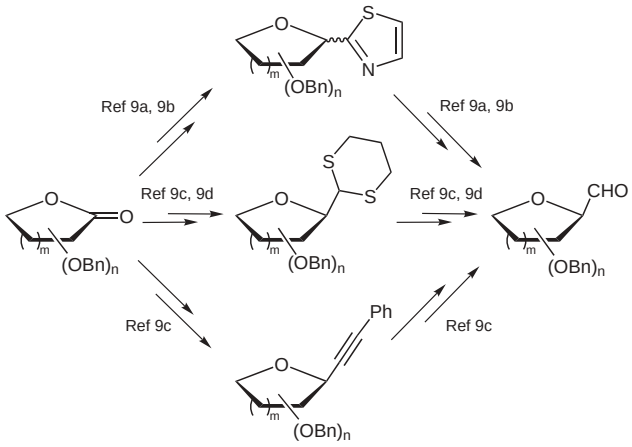
Synthesis of the Acylsilanes

We have synthesized two acylsilane representatives of the D-ribofuranose and D-glucopyranose series. The strategy was based on 1-*C*-formylglycosides as key intermediates. Different routes were reported in the literature towards these compounds starting from lactones (Scheme 1).[9]



Scheme 1

The perbenzylated D-glucono-1,5-lactone **1**[10] was converted into the corresponding 1-*C*-formyl derivative **2** according to a procedure reported by Genet's group.[9c] In our hands, the final aldehyde **2** was obtained as a 1:1 mixture with its hydrate, and all attempts to improve the purity allowed us to reach a 7:3 ratio in favor of the anhydrous form as the best result. A similar reaction sequence was applied to the perbenzylated D-ribonolactone **3**[11] to give the corresponding 1-*C*-formyl D-ribofuranoside **4**, also partially hydrated (Scheme 2).

Two different pathways were explored to convert the aldehydes into the targeted acylsilanes. The first one, described by Yoshida and co-workers for simple aldehydes,[12] was applied to the D-gluco-derivative **2**. Nucleophilic addition of the lithio derivative of bis(trimethylsilyl)methoxymethane to the aldehyde gave, via a Peterson reaction, the expected enol ether **5** and unreacted starting material which were isolated in 49% and 31% yield respectively. Then, acidic hydrolysis of **5** led to the acylsilane **6**. All attempts to improve the conversion rate of this reaction were unsuccessful even using an excess (1.5 equiv) of the nucleophile, due to the partially hydrated character of the intermediate aldehyde **2** (Scheme 3).

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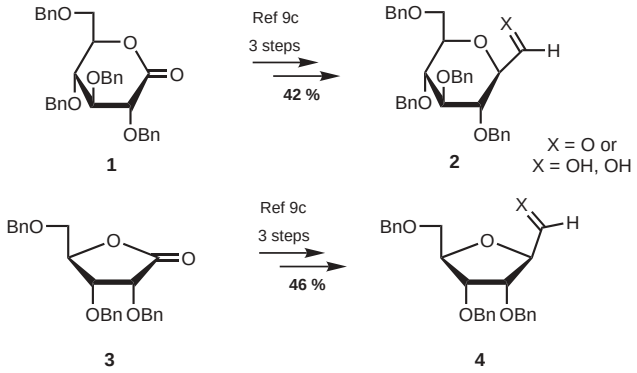
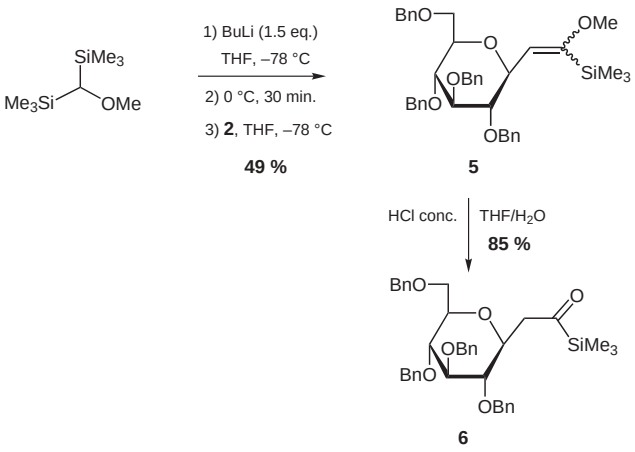
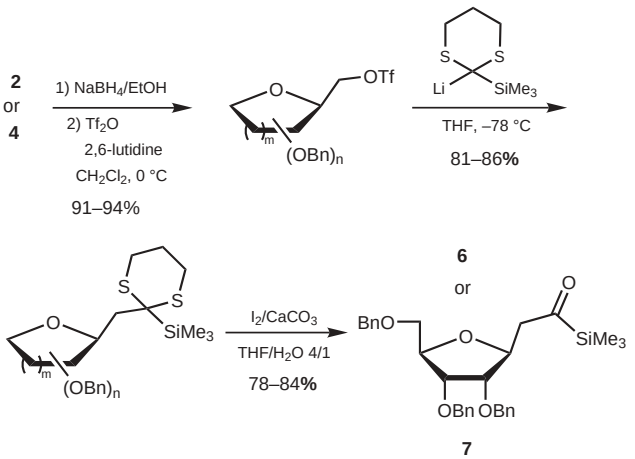


Scheme 2



Scheme 3

To overcome the problematic addition of an organometallic species to a partially hydrated aldehyde, we developed another method based on the sequence: nucleophilic substitution by 2-lithio-2-trimethylsilyl-1,3-dithiane-dethioketalization, well known in our laboratory.[13] The formyl derivatives **2** and **4** were quantitatively reduced under standard conditions. The resulting primary alcohols were converted into the corresponding triflates, which were displaced by the silylcarbonyl equivalent. Dethioketalization was efficiently performed with iodine/$CaCO_3$ in aqueous THF to give the acylsilanes **6** and **7** in good yields (Scheme 4).[14]

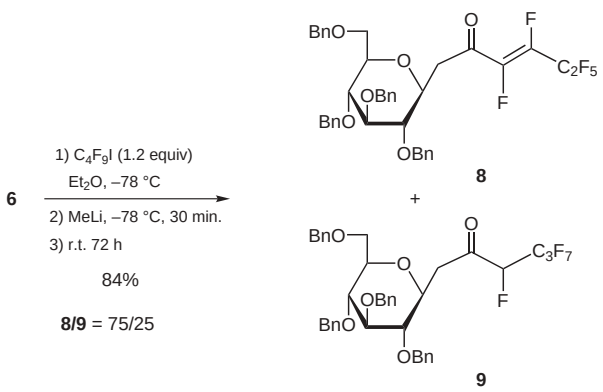


Scheme 4

Synthesis of Polyfluorinated Homo-*C*-Nucleoside Analogues

The multistep process to convert acylsilanes into fluorinated heterocycles may be performed sequentially by treating the isolated hemifluorinated enone intermediates with a bis (nucleophile) or in a one-pot operation from the acylsilanes.[6–8] The enone itself is the result of a multistep sequence starting by the reaction of the acylsilane with an in situ generated perfluoroorganolithium reagent, and involving a Brook rearrangement.[5] The direct precursor of the enone is a silylenolether, the conversion of which is generally activated by addition of triethylamine. For the synthesis presented here, no triethylamine was added and the conversion into the enone occurred under the unique action of the fluoride ion released subsequently to the Brook rearrangement.

The treatment of an ethereal solution of the pyranosic acylsilane **6** and perfluorobutyl iodide with methyllithium at low temperature then at room temperature led to the corresponding hemifluorinated enone **8** (β-anomer exclusively) and the α-hydroperfluorobutyl ketone **9** as an inseparable 75/25 mixture (total yield = 84%; Scheme 5).[15] The ketone **9** results from the hydrolysis of the remaining silylenolether. The complete stereoselectivity of the reaction seems to rule out the opening of the pyranose ring although the ring closure of the proposed enone intermediate would probably occur preferentially towards the all equatorial compound.[16] It was not necessary to optimize the reaction conditions in order to improve the enone content. The α-hydroperfluorobutyl ketone **9** is indeed a synthetic equivalent of the enone **8** owing to the easy HF elimination under the basic conditions used for heterocycles synthesis (vide infra). Hence the presence of **9** has not to be considered here as a drawback, and the subsequent reactions leading to heterocycles were performed on the mixture.



Scheme 5

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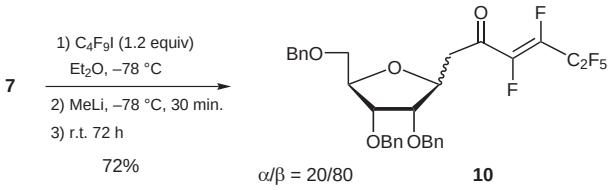
When submitted to the same reaction conditions, the D-ribofuranosic acylsilane **7** was quantitatively converted into the expected enone **10**, but some epimerization took place at the anomeric carbon, as already observed in a similar 'furanose' situation (Scheme 6).[7,17]

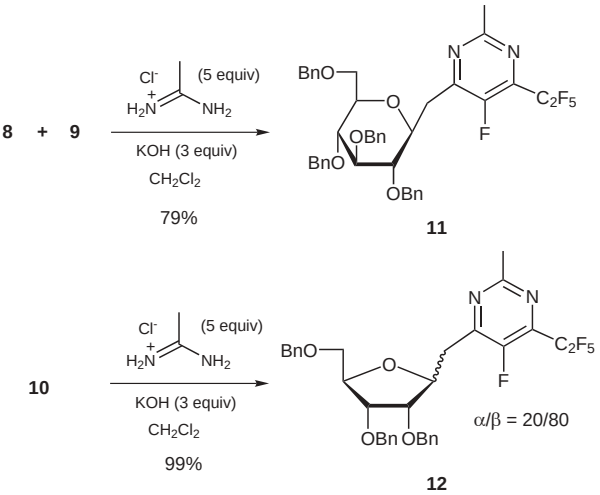


Scheme 6

This epimerization probably occurred via a retro-Michael type process. The two epimeric enones were obtained in a 80/20 ratio, the major one having the β-configuration according to a coupling constant $^3J_{3',4'}$ similar to those reported for 2,3-*O*-isopropylidene-α-D-ribofuranosyl-*C*-glycosides.[18] Several experiments gave a constant epimeric ratio (β/α = 80:20 by ^{19}F NMR), therefore assumed to represent the thermodynamic equilibrium. The β-configuration was attributed to the major isomer after comparison of the coupling constants $^3J_{3',4'}$ with those reported for 2,3-*O*-isopropylidene-α-D-ribofuranosyl-*C*-glycosides.[18]

Pyrimidine (from acetamidine) and pyrazole (from methylhydrazine) derivatives were chosen to exemplify the preparation of polyfluorinated homo-*C*-nucleosides. Whereas the pyrazole derivatives were achieved via a one-pot procedure from acylsilanes, we operated sequentially via the isolated enones to obtain satisfactory yields of the pyrimidine derivatives, as previously observed with other substrates.[7]

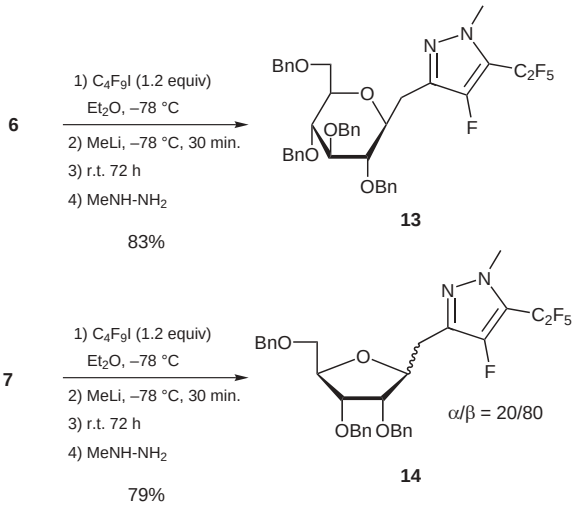
Isolated enones **8** (as a mixture with the ketone **9**, vide supra) and **10** (mixture of epimers) were reacted with acetamidine (released from its hydrochloride) to give excellent yields of the pyrimidine derivatives **11** and **12** respectively (Scheme 7).[19] The D-ribofuranose derived pyrimidine



Scheme 7

12 is an inseparable mixture of anomers in a ratio (β/α = 80:20) corresponding to the starting mixture.

The pyrazole derivatives **13** and **14**, each as a single regioisomer,[8] were prepared conveniently in high overall yield by simply adding methylhydrazine to the crude mixture from the reaction of acylsilanes **6** and **7**, respectively (Scheme 8).[20] Compound **14** was obtained as an inseparable anomeric mixture (β/α = 75:25) comparable to the corresponding enone mixture.



Scheme 8

In summary, we have developed two new routes for the synthesis of new carbohydrates-derived acylsilanes with the $COSiMe_3$ group linked to the anomeric carbon via a methylene group. These unprecedented *C*-glycosides were converted, by a sequential or a one-pot reaction with perfluoroorganolithium reagent and acetamidinium salt or methylhydrazine, into the respective pyrimidine or pyrazole derivatives. These compounds may be considered as homo-*C*-nucleoside analogues having a fluorine and a pentafluoroethyl group on vicinal positions of the base moiety. All reactions were carried out in mild and effective conditions, and the high overall yields generally obtained deserve to be emphasized owing to the multi-step process, especially for the pyrazoles one-pot synthesis.

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(14) Selected data for the acylsilanes **6** and **7**. Compound **6**: yellow syrup. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.37–7.20 (m, 20 H, H-aromatic), 4.96–4.85 (m, 4 H, H-benzyl), 3.88 (ddd, 1 H, $J_{1',2'}$ = 9.2 Hz, $J_{1',2}$ = 7.6 Hz, $J_{1',2}$ = 3.6 Hz, H-1′), 3.79–3.63 (m, 4 H, H-3′, H-4′, H-6′, H-6′), 3.47 (m, 1 H, H-5′), 3.37 (t, 1 H, $J_{2',1'} = J_{2',3'}$ = 9.2 Hz, H-2′), 2.87 (dd, 1 H, $J_{2,2}$ = 15.6 Hz, $J_{2,1'}$ = 7.6 Hz, H-2), 2.79 (dd, 1 H, $J_{2,2}$ = 15.6 Hz, $J_{2,1'}$ = 3.6 Hz, H-2), 0.31 (s, 9 H, $SiMe_3$) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 247.0 (C=O), 138.4–137.9 (C-q aromatic), 128.4–127.5 (CH aromatic), 87.2 (C-3′), 81.0 (C-2′), 78.7 (C-5′), 78.2 (C-4′), 75.5 (CH_2 benzyl), 74.9 (CH_2 benzyl), 74.8 (CH_2 benzyl), 74.6 (C-1′), 73.3 (CH_2 benzyl), 68.6 (C-6′), 49.5 (C-2), –3.4 ($SiMe_3$) ppm. MS (EI): *m/z* (%) = 638 (16) [M$^+$], 623 (32) [M – 15], 522, 517, 439 (100), 372, 279. Compound **7**: yellow syrup. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.27–7.10 (m, 15 H, H-aromatic), 4.51–4.32 (m, 7 H, 6 H-benzyl, H-1′), 4.05 (dt, 1 H, $J_{4',3'}$ = 5.2 Hz, $J_{4',5'} = J_{4',5'}$ = 3.9 Hz, H-4′), 3.77 (t, 1 H, $J_{3',2'} = J_{3',4'}$ = 5.2 Hz, H-3′), 3.49 (t, 1 H, $J_{2',3'} = J_{2',1'}$ = 5.2 Hz, H-3′), 3.40 (dd, 1 H, $J_{5',5'}$ = 10.5 Hz, $J_{5',4'}$ = 3.9 Hz, H-5′), 3.35 (dd, 1 H, $J_{5',5'}$ = 10.5 Hz, $J_{5',4'}$ = 3.9 Hz, H-5′), 2.71 (dd, 1 H, $J_{2,2}$ = 16.5 Hz, $J_{2,1'}$ = 7.0 Hz, H-2), 2.56 (dd, 1 H, $J_{2,2}$ = 16.5 Hz, $J_{2,1'}$ = 5.5 Hz, H-2), 0.20 (s, 9 H, $SiMe_3$) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 247.2 (C=O), 138.7–138.3 (C-q aromatic), 128.8–128.0 (CH aromatic), 81.5 (C-4′), 80.8 (C-2′), 77.2 (C-3′), 76.7 (C-1′), 73.8 (CH_2 benzyl), 72.2 (CH_2 benzyl), 72.1 (CH_2 benzyl), 70.5 (C-5′), 52.2 (C-2), –2.8 ($SiMe_3$) ppm. MS (EI): *m/z* (%) = 518 (26) [M$^+$], 427 (100), 337, 261, 179.

(15) **Experimental Procedure for the Synthesis of Enone 8.** To a solution, under Ar, of the acylsilane **6** (100 mg, 0.16 mmol) and perfluorobutyl iodide (32 μL, 0.19 mmol) in anhydrous Et_2O (10 mL) was added dropwise, at –78 °C, a solution of MeLi 1 M in Et_2O (190 μL, 0.19 mmol). After 30 min at –78 °C, the resulting mixture was stirred at r.t. for 3 d. The reaction was then washed with a sat. NaCl solution and the aqueous layer extracted twice with Et_2O. The organic layer was dried over $MgSO_4$, filtered and Et_2O was evaporated. The residue was purified by a silica gel column chromatography (petroleum ether/EtOAc: 95:5) to afford 99 mg (84%) of an unseparable mixture of enone **8** (75%) and the corresponding hydroperfluoroketone **9** (25%). Selected data of the mixture of enone **8** and the corresponding hydroperfluoroketone **9**. Enone **8**: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.43–7.16 (m, 20 H, H-aromatic), 5.03 (d, 1 H, *J* = 12.5 Hz, H-benzyl), 4.97 (d, 1 H, *J* = 11.5 Hz, H-benzyl), 4.91 (d, 1 H, *J* = 11.0 Hz, H-benzyl), 4.84 (d, 1 H, *J* = 11.0 Hz, H-benzyl), 4.64 (d, 1 H, *J* = 11.5 Hz, H-benzyl), 4.63 (d, 1 H, *J* = 12.0 Hz, H-benzyl), 4.54 (d, 1 H, *J* = 12.5 Hz, H-benzyl), 4.48 (d, 1 H, *J* = 12.0 Hz, H-benzyl), 3.88 (ddd, 1 H, $J_{1',2'}$ = 9.3 Hz, $J_{1',1}$ = 7.9 Hz, $J_{1',1}$ = 4.4 Hz, H-1′), 3.79–3.66 (m, 4 H, H-3′, H-4′, H-6′, H-6′), 3.50 (m, 1 H, H-5′), 3.38 (t, 1 H, $J_{2',3'} = J_{2',1'}$ = 9.3 Hz, H-2′), 2.93 (ddd, 1 H, $J_{1,2}$ = 17.1 Hz, $J_{1,1'}$ = 4.4 Hz, $^4J_{1,F}$ = 2.0 Hz, H-1), 2.85 (ddd, 1 H, $J_{1,2}$ = 17.1 Hz, $J_{1,1'}$ = 7.9 Hz, $^4J_{1,F}$ = 2.0 Hz, H-1) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 188.7 (dd, $^2J_{C,F}$ = 17.7 Hz, $^3J_{C,F}$ = 3.2 Hz, C=O), 138.7–138.1 (C-q aromatic), 129.0–128.2 (CH aromatic), 87.7 (C-3′), 80.7 (C-2′), 79.4 (C-5′), 78.6 (C-4′), 76.1 (CH_2 benzyl), 75.4 (CH_2 benzyl), 75.3 (CH_2 benzyl), 74.5 (C-1′), 73.9 (CH_2 benzyl), 68.9 (C-6′); 42.7 (d, $^3J_{C,F}$ = 1.6 Hz, C-1) ppm. ^{19}F NMR (235.4 MHz, $CDCl_3$): δ = –84.6 (m, 3 F, CF_3), –121.6 (dm, 2 F, $^3J_{F,F}$ = 14.7 Hz, CF_2), –151.8 (dm, 1 F, $^3J_{F,F}$ = 134.5 Hz, CF_2-*C*F), –152.6 (dm, 1 F, $^3J_{F,F}$ = 134.5 Hz, CO-*C*F) ppm. Hydroperfluoroketone **9** (50:50 mixture of two diastereomers): ^{19}F NMR (235.4 MHz, $CDCl_3$): δ = –81.2 (m, 3 F, CF_3), –120.3 (dm, 2 F, $^2J_{F,F}$ = 282.0 Hz, CHF-*C*F_2), –126.7 (m, 2 F, CF_2-*C*F_2), –205.3 (dm, 1 F, $^2J_{H,F}$ = 45.7 Hz, CHF) ppm.

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(17) Selected data for the mixture of enones **10**. Enone β-**10**: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.41–7.26 (m, 15 H, H-aromatic), 4.79 (d, 1 H, *J* = 11.5 Hz, H-benzyl), 4.67 (d, 1 H, *J* = 11.8 Hz, H-benzyl), 4.63 (d, 1 H, *J* = 11.8 Hz, H-benzyl), 4.58 (d, 1 H, *J* = 11.8 Hz, H-benzyl), 4.54–4.43 (m, 2 H, H-1′, H-benzyl), 4.39 (d, 1 H, *J* = 11.5 Hz, H-benzyl), 4.24 (ddd, 1 H, $J_{4',5'}$ = 4.1 Hz, $J_{1',1}$ = 3.5 Hz, $J_{1',1}$ = 3.4 Hz, H-4′), 3.96 (dd, 1 H, $J_{3',2'}$ = 5.3 Hz, $J_{3',4'}$ = 3.4 Hz, H-3′), 3.71 (dd, 1 H, $J_{2',1'}$ = 6.9 Hz, $J_{2',3'}$ = 5.3 Hz, H-2′), 3.59 (dd, 1 H, $J_{5',5'}$ = 10.6 Hz, $J_{5',4'}$ = 3.5 Hz, H-5′), 3.49 (dd, 1 H, $J_{5',5'}$ = 10.6 Hz, $J_{5',4'}$ = 4.1 Hz, H-5′), 2.96 (dm, 1 H, $J_{1,1}$ = 17.9 Hz, H-1), 2.87 (dm, 1 H, $J_{1,1}$ = 17.9 Hz, H-1) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 188.5 (dd, $^2J_{C,F}$ = 17.2 Hz, $^3J_{C,F}$ = 2.7 Hz, C=O), 137.9–137.5 (C-q aromatic), 128.4–127.6 (CH aromatic), 82.2 (C-4′), 80.4 (C-2′), 77.2 (C-3′), 75.5 (C-1′), 73.4 (CH_2 benzyl), 72.1 (CH_2 benzyl), 71.7 (CH_2 benzyl), 70.0 (C-5′), 44.2 (C-1) ppm. ^{19}F NMR (235.4 MHz, $CDCl_3$): δ = –84.6 (m, 3 F, CF_3), –121.6 (dm, 2 F, $^3J_{F,F}$ = 15.3 Hz, CF_2), –151.7 (dm, 1 F, $^3J_{F,F}$ = 137.3 Hz, CO-*C*F), –152.4 (dm, 1 F, $^3J_{F,F}$ = 137.3 Hz, CF_2-*C*F) ppm. Enone α-**10**: ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 188.4 (dd, $^2J_{C,F}$ = 17.2 Hz, $^3J_{C,F}$ = 2.7 Hz, C=O), 138.0–137.7 (C-q aromatic), 128.4–127.6 (CH aromatic), 80.1 (C-4′), 79.3 (C-2′), 77.2 (C-3′), 75.4 (C-1′), 73.6 (CH_2 benzyl), 72.7 (CH_2 benzyl), 71.7 (CH_2 benzyl), 69.9 (C-5′), 41.6 (C-1) ppm. ^{19}F NMR (235.4 MHz, $CDCl_3$): δ = –84.6 (m, 3 F, CF_3) ppm.

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(19) **Experimental Procedure for the Synthesis of the Pyrimidines 11 and 12.** To a suspension of acetamidinium chloride (5 equiv) and KOH (3 equiv) in CH_2Cl_2 (15 mL) stirred for 1 h, was added a solution of the mixture of enone **8** and the corresponding hydroperfluoroketone **9** or the mixture of enones **10** (1 equiv) in CH_2Cl_2 (2 mL). After 24 h at r. t., the reaction was washed with a sat. NaCl solution and the aqueous layer extracted twice with CH_2Cl_2. The organic layer was dried over $MgSO_4$, filtered and the solvent was evaporated. The residue was purified by a silica gel column chromatography (petroleum ether/EtOAc: 90:10). Selected data of pyrimidine **11**: yellow syrup (79%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.35–7.00 (m, 20 H, H-aromatic), 4.95–4.35 (m, 8 H, H-benzyl), 3.70–3.40 (m, 6 H, H-1′, H-3′, H-4′, H-5′, H-6′, H-6′), 3.33 (t, 1 H, $J_{2',3'} = J_{2',1'}$ = 9.3 Hz, H-2′), 3.00 (dd, 1 H, $J_{1,1}$ = 15.1 Hz, $J_{1,1'}$ = 3.0 Hz, H-1), 2.80 (dd, 1 H, $J_{1,1}$ = 15.1 Hz, $J_{1,1'}$ = 6.9 Hz, H-1), 2.68 (s, 3 H, CH_3) ppm. ^{19}F NMR (235.4 MHz, $CDCl_3$): δ = –83.9 (m, 3 F, CF_3), –117.4 (dm, 2 F, $^4J_{F,F}$ = 19.0 Hz, CF_2), –139.8 (m, 1 F, CF) ppm. Selected data of pyrimidine **12**: yellow syrup (99%, α/β = 20:80), β-anomer **12**: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.38–7.23 (m, 15 H, H-aromatic), 4.63–4.45 (m, 7 H, 6 H-benzyl, H-1′), 4.20 (ddd, 1 H, $J_{4',3'}$ = 4.2 Hz, $J_{4',5'}$ = 4.1 Hz, $J_{4',5'}$ = 3.5 Hz, H-4′), 3.95 (t, 1 H, $J_{3',2'} = J_{3',4'}$ = 4.2 Hz, H-3′), 3.81 (dd, 1 H, $J_{2',1'}$ = 5.9 Hz, $J_{2',3'}$ = 4.2 Hz, H-2′), 3.56 (dd, 1 H, $J_{5',5'}$ = 10.7 Hz, $J_{5',4'}$ = 3.5 Hz, H-5′), 3.51 (dd, 1 H, $J_{5',5'}$ = 10.7 Hz, $J_{5',4'}$ = 4.1 Hz, H-5′), 3.16 (dd, 1 H, $J_{1,1}$ = 14.0 Hz, $J_{1,1'}$ = 7.1 Hz, H-1), 3.11 (dd, 1 H, $J_{1,1}$ = 14.0 Hz, $J_{1,1'}$ = 5.4 Hz, H-1), 2.70 (s, 3 H, CH_3) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 163.4 (d, $^2J_{C,F}$ = 9.9 Hz, C-4), 158.5 (d, $^2J_{C,F}$ = 15.3 Hz, C-6), 153.2 (d, $^1J_{C,F}$ = 273.8 Hz, C-5), 138.0–137.8 (C-q aromatic), 128.3–127.5 (CH aromatic), 118.1 (tq, $^1J_{C,F}$ = 287.4 Hz, $^2J_{C,F}$ = 35.6 Hz, CF_3), 82.0 (C-4′), 80.6 (C-2′), 78.3 (C-1′), 77.0 (C-3′), 73.3 (CH_2 benzyl), 72.0 (CH_2 benzyl), 71.8 (CH_2 benzyl), 70.2 (C-5′), 35.2 (CH_2), 25.0 (CH_3) ppm. ^{19}F NMR (235.4 MHz, $CDCl_3$): δ = –83.5 (m, 3 F, CF_3), –117.4 (d, 2 F, $^4J_{F,F}$ = 21.5 Hz, CF_2), –139.4 (m, 1 F, CF) ppm. α-Anomer **12**: ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 163.2 (d, $^2J_{C,F}$ = 9.2 Hz, C-4), 160.0 (d, $^2J_{C,F}$ = 14.5 Hz, C-6), 80.5 (C-4′), 79.1 (C-3′), 77.9 (C-1′), 77.8 (C-2′), 73.0 (CH_2 benzyl), 72.6 (CH_2 benzyl), 72.0 (CH_2 benzyl), 70.0 (C-5′), 25.1 (CH_3) ppm.^{19}F NMR (235.4 MHz, $CDCl_3$): δ = –117.5 (dm, 2 F, $^4J_{F,F}$ = 21.5 Hz, CF_2), –139.2 (m, 1 F, CF) ppm.

(20) **Experimental Procedure for the Synthesis of the Pyrazoles 13 and 14.** To a solution, under Ar, of the acylsilane **6** or **7** (1 mmol) and perfluorobutyl iodide (1.2 mmol) in anhydrous Et_2O (15 mL) was added dropwise, at –78 °C, a solution of MeLi 2.2 M in Et_2O (1.2 mmol). After 30 min at –78 °C, the resulting mixture was stirred at r.t. for 3 d. Methylhydrazine (5 mmol) was then added and the reaction was monitored by TLC (petroleum ether/EtOAc 85:15). After 18 h at r.t., the reaction was washed with a sat. NaCl solution and the aqueous layer extracted twice with Et_2O. The organic layer was dried over $MgSO_4$, filtered and ether was evaporated. The residue was purified by a silica gel column chromatography (petroleum ether/EtOAc: 90:10). Selected data of pyrazole **13**: yellow syrup (83%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.33–7.04 (m, 20 H, H-aromatic), 4.92–4.67 (m, 4 H, H-benzyl), 4.59–4.35 (m, 4 H, H-benzyl), 3.72 (s, 3 H, NCH_3), 3.70–3.45 (m, 6 H, H-1′, H-3′, H-4′, H-5′, H-6′, H-6′), 3.32 (t, 1 H, $J_{2',3'} = J_{2',1'}$ = 8.7 Hz, H-2′), 3.04 (dd, 1 H, $J_{1,1}$ = 14.8 Hz, $J_{1,1'}$ = 3.3 Hz, H-1), 2.77 (dd, 1 H, $J_{1,1}$ = 14.8 Hz, $J_{1,1'}$ = 7.3 Hz, H-1) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 146.9 (d, $^1J_{C,F}$ = 260.6 Hz, C-4), 138.4–138.1 (C-q aromatic), 137.9 (d, $^2J_{C,F}$ = 9.7 Hz, C-5), 135.2 (d, $^2J_{C,F}$ = 9.7 Hz, C-3), 128.5–127.9 (CH aromatic), 117.5 (tq, $^1J_{C,F}$ = 287.4 Hz, $^2J_{C,F}$ = 35.6 Hz, CF_3), 87.2 (C-3′), 81.3 (C-2′), 79.2 (C-5′), 78.5 (C-4′), 77.4 (C-1′), 75.6 (CH_2 benzyl), 75.0 (CH_2 benzyl), 74.9 (CH_2 benzyl), 73.4 (CH_2 benzyl), 68.8 (C-6′), 39.7 (CH_2), 29.7 (NCH_3) ppm. ^{19}F NMR (235.4 MHz, $CDCl_3$): δ = –85.5 (m, 3 F, CF_3), –113.3 (dm, 2 F, $^4J_{F,F}$ = 11.7 Hz, CF_2), –166.9 (m, 1 F, CF) ppm. Selected data of pyrazole **14**: yellow syrup (100%, α/β = 25:75). β-Anomer: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.42–7.20 (m, 15 H, H-aromatic), 4.65–4.42 (m, 7 H, 6 H-benzyl, H-1′), 4.23 (m, 1 H, H-4′), 3.90 (t, 1 H, $J_{3',2'} = J_{3',4'}$ = 5.6 Hz, H-3′), 3.73 (t, 1 H, $J_{2',3'} = J_{2',1'}$ = 5.6 Hz, H-2′), 3.70 (s, 3 H, NCH_3), 3.56 (dd, 1 H, $J_{5',5'}$ = 10.9 Hz, $J_{5',4'}$ = 3.4 Hz, H-5′), 3.48 (dd, 1 H, $J_{5',5'}$ = 10.9 Hz, $J_{5',4'}$ = 5.3 Hz, H-5′), 2.92 (dm, 1 H, $J_{1,1}$ = 14.9 Hz, H-1), 2.85 (dm, 1 H, $J_{1,1}$ = 14.9 Hz, H-1) ppm. ^{19}F NMR (235.4 MHz, $CDCl_3$): δ = –85.4 (m, 3 F, CF_3), –113.2 (dm, 2 F, $^4J_{F,F}$ = 12.5 Hz, CF_2), –167.3 (m, 1 F, CF) ppm. α-Anomer: ^{19}F NMR (235.4 MHz, $CDCl_3$): δ = –85.1 (m, 3 F, CF_3), –113.1 (dm, 2 F, $^4J_{F,F}$ = 12.5 Hz, CF_2), –167.7 (m, 1 F, CF) ppm.

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