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# Synthesis of nucleosides from 4-methylidenefuranoses: a non-classical electrophilic addition

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**Abstract**—The reaction of persilylated bases (thymine, uracil, cytosine, and 5-fluorouracil) with either 3-*O*-benzoyl-5-deoxy-1,2-*O*-isopropylidene-α-D-*erythro*-pent-4-enofuranose **6** or its 3-*O*-benzyl analogue **7** in the presence of *N*-iodosuccinimide (NIS) afforded two types of product with high stereoselectivity; either (1′*S*,2′*R*,3′*S*)-3′-*O*-benzoyl- **8**–**10** or -3′-*O*-benzyl-5′-deoxy-5′-iodo-1′,2′-*O*-isopropylidene-4′-oxo-1′-yl-pyrimidines **11**–**13**, respectively, from 1,4-addition with participation of the oxygen atom at the furanoid ring, and either 3′-*O*-benzoyl- **14**–**16**, or 3′-*O*-benzyl-5′-deoxy-5′-iodo-1′,2′-*O*-isopropylidene-β-L-*lyxo*-4′-yl-pyrimidine and **17**–**19** resulting from normal electrophilic addition at the exocyclic methylene group. A third compound was isolated from the reaction of **7** with persilylated uracil/NIS and identified as the doubly *N*,*N*′-glycosylated pyrimidine **20**. 

## 1. Introduction

In previous papers[1] we reported on the highly regio- and stereoselective synthesis of nucleosides from the reaction of furanoid glycals with persilylated bases in the presence of NIS. On the basis of the excellent results obtained in our previous studies, we have explored the same methodology but on an activated enol ether-like exocyclic methylene group in order to prepare nucleoside structurally related with the angustmycin A.[2]

## 2. Results and discussion

Reaction of 1,2-*O*-isopropylidene-α-D-xylofuranose[3] **1** with $I_2/Ph_3P$/imidazole in anhydrous dichloromethane according to the Garegg–Samuelson procedure[4] proceeded with high regioselectivity to afford 5-deoxy-5-iodo-1,2-*O*-isopropylidene-α-D-xylofuranose **2**.[5] Compound **2** was transformed into its 3-epimer **3**[6] (α-D-*ribo*) by a well established protocol consisting of PCC oxidation of **2** to the corresponding ald-3-ulose and subsequent sodium borohydride reduction.[7] Compound **3** was then straightforwardly 3-*O*-protected as its benzoyl **4** or benzyl **5**[8] derivative, in the usual manner. 4,5-Dehydrohaloganation of either **4** or **5** by classical methods in order to obtain the related 4-methylenefuranoses **6**[9] or **7** occurred in moderate or very low yields, but treatment with caesium fluoride afforded the required compounds in excellent yield (Scheme 1).

Compounds **6** and **7** (see Scheme 2) have all substituents at the α-face and it can be expected that any electrophilic attack at the exocyclic methylene group must occur to the less hindered β-face in order to produce the intermediate cyclic iodonium ion A that would be attacked with high regio- and stereoselectivity at C(4) by the persilylated base (PSB) at the α-face to afford the related *N*-nucleosides. Nevertheless, when **6** and **7** were allowed to react with NIS, two unexpected products were isolated from the reaction mixtures, either **8**–**13**, probably formed via S*N*1 *anti* approach of the PSB at C(1) with respect to the C(2) substituent of the stabilized oxocarbenium intermediate D (see Scheme 2), or those from similar attack by the PSB at the less hindered β-face, but at C(4) of the stabilized oxocarbenium ion B. To the best of our knowledge, there is no previous report in the literature about such processes, although related processes where alkenyl glycopyranosides and different promoters were used for glycosidations are known.[10]

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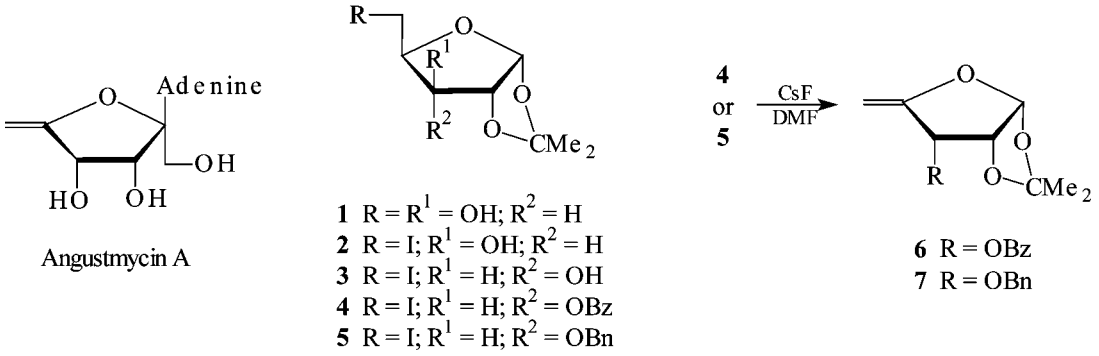
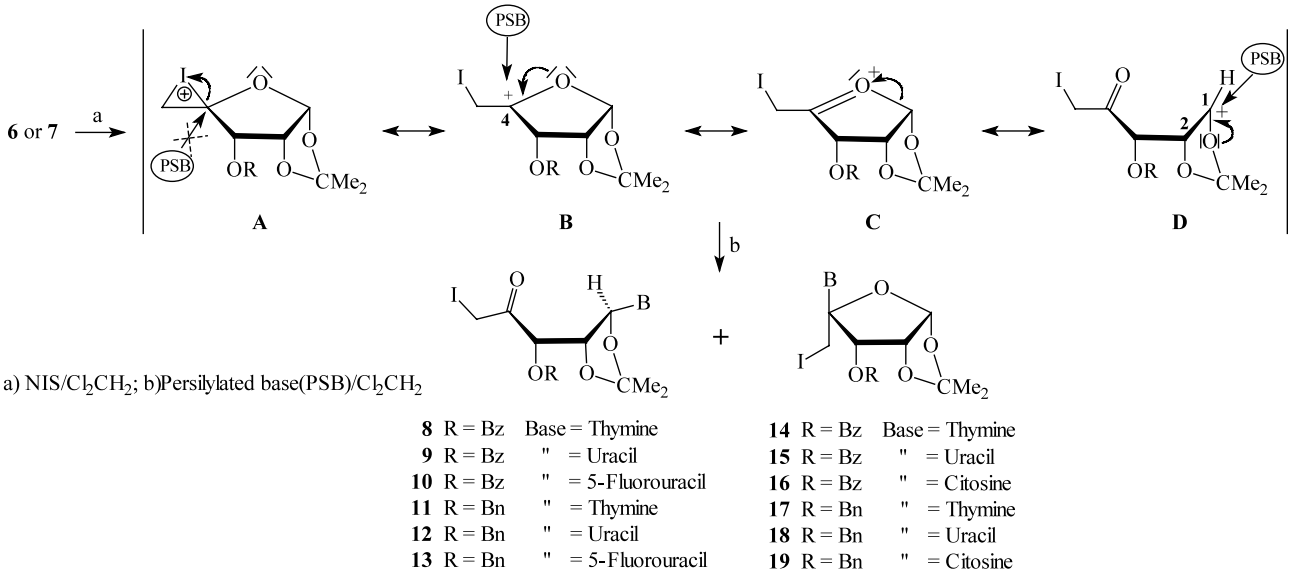



**Scheme 1.**




**Scheme 2.**

Our results could be explained on the basis of the different nucleophilic character of the bases. Thus, the most nucleophilic cytosine reacted giving only **16** and **19**, whereas the less nucleophilic 5-fluorouracil afforded only **10** and **13**. The other bases, which have moderate nucleophilic character (uracil and thymine) produced mixtures of both types of product.

The structures for compounds **8**–**13** and **14**–**19** were established on the basis of their analytical and spectroscopic data, and the stereochemistry of the new C(1′) and C(4′) stereogenic centres was determined by NOESY experiments. As an example, the definite NOE effect between C(2′)H and C(6)H of thymine in **8** and **11**, as well as C(1′)H and C(6)H of thymine in **14** and **17**, indicates that the base and the mentioned protons are in a *cis* disposition (see Fig. 1 below) in the 1,3-dioxolane and furanose ring, respectively.

The presence of the iodomethylketone function (C(4′) and C(5′) at 200 and 5 ppm, respectively) in compounds **8**–**13** was demonstrated by catalytic hydrogenation of **10** to the corresponding methylketone **21** (as evidenced by NMR analyses).

Finally, the reaction of **7** with persilylated uracil afforded a third *N*,*N*′-dialkylated compound **20**, isolated in 23% yield. The analytical and spectroscopic data allowed its complete structural elucidation. Thus, in a HMBC experiment on **20**, H-1″ of the sugar residue (6.62 ppm) (see Fig. 2) showed two strong interactions with C(2) (149.5 ppm) and C(4) (162.6 ppm) of the ring, indicating that the open sugar moiety was linked to N(3).

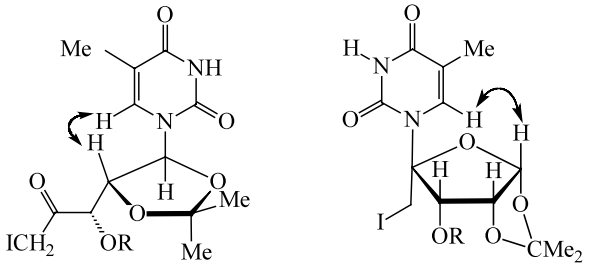


**Figure 1.** NOE interaction for **8** and **14** (R = Bz), and **11** and **17** (R = Bn).

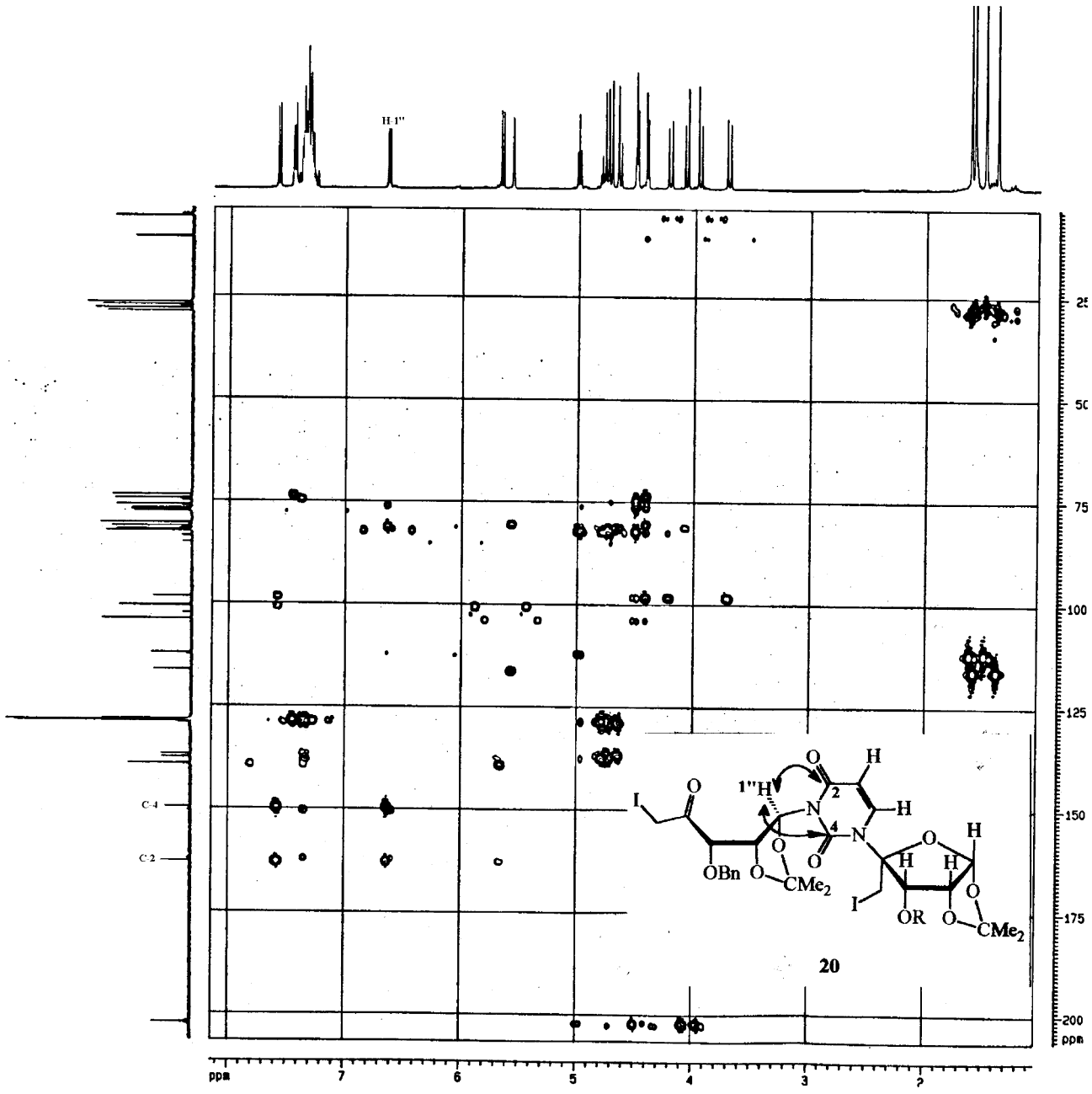



**Figure 2.** HMBC experiment on **20**.

## 3. Experimental

### 3.1. General

Solutions were dried over $MgSO_4$ before concentration under reduced pressure. The $^1H$ and $^{13}C$ NMR spectra were recorded with Bruker AMX-300, AM-300, and ARX-400 spectrometers for solutions in $CDCl_3$ (internal $Me_4Si$). IR spectra were recorded with a Perkin–Elmer 782 instrument and mass spectra with a Micromass Mod. Platform II and Autospec-Q mass spectrometers. Optical rotations were measured for solutions in $CHCl_3$ (1 dm tube) with a Jasco DIP-370 polarimeter. TLC was performed on precoated silica gel 60 $F_{254}$ aluminium sheets and detection was by charring with $H_2SO_4$. Column chromatography was performed on silica gel (Merck, 7734).

### 3.2. 5-Deoxy-5-iodo-1,2-*O*-isopropylidene-α-D-xylofuranose 2

To a stirred solution of 1,2-*O*-isopropylidene-α-D-xylofuranose **1** (4.3 g, 22.6 mmol) in anhydrous dichloromethane (200 mL) were added iodine (14.35 g, 56.5 mmol), triphenylphosphine (14.8 g, 56.5 mmol), and imidazole (8.6 g, 120 mmol) and the mixture was heated under reflux for 8 h. TLC (ether–hexane, 3:1) then revealed the presence of a new compound of higher mobility. The reaction mixture was washed with diluted aqueous hydrochloric acid and water until neutral pH was reached, then concentrated and the residue was chromatographed (ether–hexane, 1:1) to afford **2** as a foam (6.6 g, 97%); $[\alpha]_D^{25}$ −38.4 (*c* 1), [lit.[5] $[\alpha]_D^{20}$ −38 (*c* 1.07, chloroform)]. $^{13}C$ NMR spectrum (100 MHz):

112.2 ($C$Me$_2$), 105.6 (C-1), 85.1, 80.8, and 75.0 (C-2,3,4), 26.9 and 26.3 (C$Me_2$), and −1.1 (C-5). The $^1$H NMR (400 MHz) spectroscopic data for **2** were identical to those already reported.[5]

### 3.3. 5-Deoxy-5-iodo-1,2-*O*-isopropylidene-α-D-ribofuranose 3

To a stirred solution of **2** (5 g, 15.8 mmol) in anhydrous dichloromethane (100 mL) were added molecular sieve (4 Å powder, 10 g) and pyridinium chlorochromate (10 g, 4.58 mmol). Stirring was maintained at room temperature overnight. TLC (ether–hexane, 3:1) then revealed a new product of higher mobility. The mixture was diluted with ether (300 mL), filtered through silica gel G and concentrated to a residue that was chromatographed (ether) to afford a compound that was not investigated but reduced at −25°C in anhydrous methanol (75 mL) by portion addition of sodium borohydride (1 g, 26.3 mmol) over 1 h. The mixture was neutralised with acetic acid and concentrated to a residue that was partitioned between dichloromethane–water. The organic phase was separated and concentrated to a residue that was submitted to column chromatography (ether–hexane, 2:1) to afford crystalline **3** as a colourless powder (4 g, 80%); mp 84–85°C; $[\alpha]_D^{22}$ +36.7 ($c$ 1), [lit.:[6] mp 84–85°C; $[\alpha]_D^{25}$ +20.6 ($c$ 0.5, chloroform)]. $^1$H NMR data: (400 MHz): 5.83 (d, 1H, $J_{1,2}=3.9$ Hz, H-1), 4.60 (dd, 1H, $J_{2,3}=5.1$ Hz, H-2), 3.75 (ddd, 1H, $J_{3,4}=10.5$, $J_{4,5a}=8.1$, $J_{4,5b}=5.6$ Hz, H-4), 3.57–3.52 (m, 2H, H-5a,3), 3.34 (dd, 1H, $J_{5a,5b}=12.0$ Hz, H-5b), 2.45 (d, 1H, $J_{3,OH}=10.5$ Hz, HO-3), 1.56 and 1.36 (2s, 6H, CMe$_2$); $^{13}$C NMR (100 MHz): 112.2 ($C$Me$_2$), 103.0 (C-1), 78.5 and 77.8 (C-2,3), 75.2 (C-4), 26.2 (C$Me_2$), and 6.4 (C-5).

### 3.4. 3-*O*-Benzoyl-5-deoxy-5-iodo-1,2-*O*-isopropylidene-α-D-ribofuranose 4

Conventional benzoylation of **3** (4 g, 13.3 mmol) with benzoyl chloride (2.3 mL, 20 mmol) and triethylamine (5.5 mL, 40 mmol) in anhydrous dichloromethane (75 mL) for 4 h, and quenching with methanol for 30 min, gave after usual work-up and column chromatography (ether–hexane, 1:4) colourless crystalline **4** (5.4 g, 93%); mp 60–61°C; $[\alpha]_D^{25}$ +111.6 ($c$ 1.02); $\nu^{KBr}_{max}$ 1745 (C=O, benzoate) and 1275 cm$^{-1}$ (CMe$_2$). $^1$H NMR data: (400 MHz), 8.08 (dd, 2 H, $J_{o\text{-},m\text{-}}=6.28$, $J_{o\text{-},p\text{-}}=1.10$ Hz, H-*ortho*), 7.60 (tt, 1H, $J_{m\text{-},p\text{-}}=6.9$ Hz, H-*para*), 7.47 (dt, 2H, H-*meta*), 5.92 (d, 1H, $J_{1,2}=3.8$ Hz, H-1), 4.98 (t, 1H, H-2), 4.81 (dd, 1H, $J_{2,3}=4.9$, $J_{3,4}=8.6$ Hz, H-3), 4.16 (dt, 1H, H-4), 3.52 (dd, 1H, $J_{4,5a}=4.2$, $J_{5a,5b}=11.1$, Hz, H-5a), 3.37 (dd, 1H, $J_{4,5b}=4.9$ Hz, H-5b), 1.55 and 1.33 (2s, 6H, CMe$_2$); $^{13}$C NMR (100 MHz), 165.7 (C=O), 133.6, 130.6, 129.2, 128.6 (Ph), 113.4 ($C$Me$_2$), 104.2 (C-1), 77.9, 76.8, and 76.4 (C-2,3,4), 26.8 (C$Me_2$), and 5.2 (C-5). Mass spectrum (LSIMS): $m/z$: 427.0023 [M$^+$+Na] for $C_{15}H_{17}O_5INa$ 427.0018 (deviation −1.0 ppm). Anal. calcd for $C_{15}H_{17}O_5I$: C, 44.57; H, 4.24. Found: C, 44.64; H, 4.59%.

### 3.5. 3-*O*-Benzyl-5-deoxy-5-iodo-1,2-*O*-isopropylidene-α-D-ribofuranose 5

To an ice-water cooled and stirred solution of **3** (3 g, 10 mmol) in anhydrous THF (50 mL) were added benzyl bromide (1.2 mL, 50 mmol) and 60% oil dispersion sodium hydride (1 g, 25 mmol) portionwise over 30 min. The reaction mixture was then stirred for an additional 2 h. The reaction was quenched by cautious addition of methanol (5 mL) and allowed to reach room temperature. The solvents were removed and the residue was partitioned between dichloromethane–water. The organic phase was separated and concentrated to a residue that was submitted to column chromatography (ether–hexane, 1:6→1:1) to afford pure **5**[8] as a colourless syrup (3.7 g, 95%); $[\alpha]_D^{24}$ +99 ($c$ 1.20), [lit.:[8b] $[\alpha]_D^{20}$ +84.9 ($c$ 4.7, dichloromethane)]. $^1$H NMR data: (300 MHz), 7.40–7.30 (m 5H, PhCH$_2$), 5.74 (d, 1H, $J_{1,2}=3.6$ Hz, H-1), 4.67 (2d, 2H, $J=11.9$ Hz, PhCH$_2$), 4.56 (pt, 1H, $J_{2,3}=4.3$ Hz, H-2), 3.73 (ddd, 1H, $J_{3,4}=8.5$, $J_{4,5a}=3.0$, $J_{4,5b}=4.3$ Hz, H-4), 3.59 (dd, 1H, H-3), 3.51 (dd, 1H, $J_{5a,5b}=11.2$, Hz, H-5a), 3.29 (dd, 1H, H-5b), 1.59 and 1.35 (2s, 6H, CMe$_2$); $^{13}$C NMR (80 MHz), 137.3, 128.6, 128.3, and 128.1 (Ph), 113.3 ($C$Me$_2$), 104.0 (C-1), 81.7 (C-3), 77.4 and 76.3 (C-2,4), 72.4 (Ph$C$H$_2$), 26.7 and 26.6 (C$Me_2$), and 7.4 (C-5).

### 3.6. Typical experimental procedure for the preparation of 4-methylidenefuranoses 6 and 7

To a stirred solution of **4** or **5** (1 mmol) in dry DMF (10 mL) was added caesium fluoride (304 mg, 2 mmol) and the mixture was heated at 120°C for either 4 or 8 h, respectively. Most of the solvent was evaporated under vacuum and the residue was partitioned into toluene–water. The organic phase was separated and concentrated to give a residue that was chromatograph (ether–hexane, 1:5) to afford crystalline **6** and syrupy **7** (82%, in both cases), respectively.

**3.6.1. 3-*O*-Benzoyl-5-deoxy-1,2-*O*-isopropylidene-α-D-*erythro*-pent-4-enofuranose 6**. Mp 54–55°C (from ether–hexane); $[\alpha]_D^{21}$ +151.6 ($c$ 1.1); $\nu^{KBr}_{max}$ 2990, 1720 (C=O, benzoate), 1680 (C=C), 1385 and 1375 cm$^{-1}$ (CMe$_2$). $^1$H NMR data (inter alia): (400 MHz), 6.02 (d, 1H, $J_{1,2}=3.6$ Hz, H-1), 5.57 (dt, 1H, $J_{2,3}=5.3$, $J_{3,5a}=2.2$, $J_{3,5b}=2.2$ Hz, H-3), 4.99 (dd, 1H, H-2), 4.62 (dt, 1H, $J_{5a,5b}=2.4$, Hz, H-5a), and 4.31 (t, 1H, H-5b); $^{13}$C NMR (100 MHz), 165.8 (C=O), 156.8 (C-4), 114.5 ($C$Me$_2$), 105.1 (C-1), 84.8 (C-5), 77.6 and 72.1 (C-2,3), 27.9 and 27.5 (C$Me_2$). Mass spectrum (LSIMS): $m/z$: 299.0894 [M$^+$+Na] for $C_{15}H_{16}O_5Na$ 299.0895 (deviation +0.4 ppm). Anal. calcd for $C_{15}H_{16}O_5$: C, 65.20; H, 5.83. Found: C, 65.05; H, 5.94%.

**3.6.2. 3-*O*-Benzyl-5-deoxy-1,2-*O*-isopropylidene-α-D-*erythro*-pent-4-enofuranose 7**. $[\alpha]_D^{25}$ +98.9 ($c$ 1.1); $\nu^{film}_{max}$ 2990, 1680 (C=C), 1385 and 1375 cm$^{-1}$ (CMe$_2$). $^1$H NMR data (inter alia): (400 MHz), 5.80 (d, 1H, $J_{1,2}=3.3$ Hz, H-1), 4.84 and 4.68 (2d, 2H, $J=12.4$, CH$_2$Ph), 4.56 (t, 1H, $J_{2,3}=3.8$, H-2), 4.48 (bs, 1H, H-5a), 4.30 (t, 1H, $J_{5a,5b}=1.8$ Hz, H-5b), 4.28 (m, 1H, $J_{3,5a}=2.1$,

$J_{3,5b}$ = 2.2 Hz, H-3), 1.54 and 1.41 (2s, 6H, $CMe_2$); $^{13}C$ NMR (100 MHz), 158.8 (C-4), 137.4, 128.5, 128.1, and 128.0 (Ph), 114.8 ($CMe_2$), 104.3 (C-1), 83.9 (C-5), 77.4 and 76.9 (C-2,3), 72.4 ($CH_2Ph$), 27.9 and 27.3 ($CMe_2$). Mass spectrum (LSIMS): $m/z$: 262.1281 [$M^+$+H] for $C_{15}H_{19}O_4$ 263.1283 (deviation +0.8 ppm).

### 3.7. Typical experimental procedure for nucleosidation of 6 and 7

A solution of persilylated base (thymine, uracil, cytosine, or 5-fluorouracil, 4 mmol) in anhydrous dichloromethane (50 mL) was added to a flask containing either **6** or **7** (3 mmol), and to the resulting stirred and cooled (ice-water) solution was added NIS (675 mg, 13 mmol) and the reaction mixture was left for 18 h. During this time the reaction mixture was allowed to reach room temperature. The solvent was evaporated and the residue submitted to column chromatography (ether–hexane, 2:1→ether in all cases, except with cytosine where dichloromethane–methanol, 20:1, was used as eluent) to afford, first compounds **8**–**13** and secondly compounds **14**–**19**, respectively, all of them slightly contaminated with succinimide ($^1H$ NMR evidence). This could be removed by dissolving in dichloromethane and washing with a saturated aqueous sodium hydrogen carbonate solution and water to give the corresponding pure compounds.

Compound **8**: (253 mg, 16%) solid foam; $[\alpha]_{405}^{24}$ −93.2 (*c* 0.93); $\nu^{film}_{max}$ 1690 (C=O) and 1260 $cm^{-1}$. For NMR data, see Tables 1 and 2. Mass spectrum (LSIMS): $m/z$: 551.0296 [$M^+$+Na] for $C_{20}H_{21}N_2O_7INa$ 551.0291 (deviation −0.9 ppm). Anal. calcd for $C_{20}H_{21}N_2O_7I$: C, 45.47; H, 4.00; N, 5.30. Found: C, 45.28; H, 3.81; N, 5.37%.

Compound **9**: (107 mg, 7%) solid foam; $[\alpha]_D^{25}$ −5.5 (*c* 1); $\nu^{film}_{max}$ 2960, 1690 (C=O), 1660, and 1250 $cm^{-1}$. For NMR data, see Tables 1 and 2. Mass spectrum (LSIMS): $m/z$: 537.0125 [$M^+$+Na] for $C_{19}H_{19}N_2O_7INa$ 537.0134 (deviation +1.8 ppm). Anal. calcd for $C_{19}H_{19}N_2O_7I$: C, 44.37; H, 3.72; N, 5.44. Found: C, 44.69; H, 3.98; N, 5.38%.

Compound **10**: (1.2 g, 75%) solid foam; $[\alpha]_D^{26}$ −14.4 (*c* 1.1); $\nu^{film}_{max}$ 3060, 1720 (C=O), 1700, and 1250 $cm^{-1}$.

**Table 1.** $^1H$ NMR chemical shifts ($\delta$) and *J* (Hz) values for compounds **8**–**13**

| Compound | H-1′ | H-2′ | H-3′ | H-5′a | H-5′b | H-3 | H-5 | H-6 | Me | $CMe_2$ |
|---|---|---|---|---|---|---|---|---|---|---|
| **8**[a] | 6.32d | 4.54dd | 6.17d | 4.25d | 4.04d | 9.24s | – | 7.19d | 1.96d | 1.55 |
| | $J_{1',2'}$ 6.6 | $J_{2',3'}$ 4.1 | | $J_{5'a,5'b}$ 11.5 | | | | | | 1.38 |
| **9**[b] | 6.34d | 4.59dd | 6.23d | 4.28d | 4.07d | 8.61s | 5.87d | 7.47d | – | 1.58 |
| | $J_{1',2'}$ 6.4 | $J_{2',3'}$ 3.8 | | $J_{5'a,5'b}$ 11.5 | | | $J_{5,6}$ 8.2 | | | 1.44 |
| **10**[b] | 6.28dd | 4.55dd | 6.24d | 4.23d | 4.02d | 8.92d | – | 7.47d | – | 1.56 |
| | $J_{1',2'}$ 6.4 | $J_{2',4'}$ 3.5 | | $J_{5'a,5'b}$ 11.4 | | $J_{3,F}$ 4.5 | | $J_{6,F}$ 5.7 | | 1.39 |
| | $J_{1',F}$ 1.6 | | | | | | | | | |
| **11**[b] | 6.23d | 4.33dd | 4.65d | 4.25d | 3.91d | 8.95s | – | 7.14s | 1.92 | 1.53 |
| | $J_{1',2'}$ 6.4 | $J_{2',3'}$ 4.2 | | $J_{5'a,5'b}$ 10.7 | | | | | | 1.47 |
| **12**[a] | 6.20d | 4.37dd | 4.70d | 4.27d | 3.92d | 9.50s | 5.78d | 7.37m* | – | 1.51 |
| | $J_{1',2'}$ 6.2 | $J_{2',3'}$ 3.8 | | $J_{5'a5'b}$ 10.6 | | | $J_{5,6}$ 8.2 | | | 1.50 |
| **13**[a] | 6.17dd | 4.36dd | 4.69d | 4.26d | 3.90d | 9.23s | – | 7.39m* | – | 1.53 |
| | $J_{1',2'}$ 6.3 | $J_{2',3'}$ 3.7 | | $J_{5'a,5'b}$ 10.6 | | | | | | 1.50 |
| | $J_{1',F}$ 1.4 | | | | | | | | | |

[a] Recorded at 400 MHz.
[b] Recorded at 300 MHz.
*Signals overlapping with those of benzyl group and also containing the coupling with fluorine.

**Table 2.** $^{13}C$ NMR chemical shifts ($\delta$) for compounds **8**–**13**

| Compound | C(2) | C(4) | C(5) | C(6) | C(1′) | C(2′) | C(3′) | C(4′) | C(5′) | Me |
|---|---|---|---|---|---|---|---|---|---|---|
| **8**[a] | 150.7 | 164.9 | 111.5 | 134.2 | 82.7 | 79.5 | 73.4 | 198.6 | 4.2 | 12.9 |
| **9**[b] | 150.3 | 164.9 | 103.5 | 138.6 | 83.3 | 80.1 | 73.5 | 198.4 | 3.8 | – |
| **10**[b] | 149.0 | 156.0[c] | 141.0[d] | 122.8[e] | 83.2 | 80.1 | 73.4 | 198.6 | 3.7 | – |
| **11**[b] | 150.5 | 163.4 | 111.4 | 134.4 | 83.5 | 80.3 | 81.1 | 202.5 | 4.9 | 12.8 |
| **12**[a] | 150.5 | 163.1 | 103.1 | 138.9 | 83.8 | 80.3 | 81.7 | 202.6 | 4.8 | – |
| **13**[a] | 149.0 | 156.5[f] | 140.8[g] | 123.1[h] | 83.7 | 80.0 | 81.5 | 202.6 | 4.7 | – |

[a] Recorded at 100 MHz.
[b] Recorded at 80 MHz.
[c] $J_{C\text{-}4,F}$ = 26.6 Hz.
[d] $J_{C\text{-}5,F}$ = 239.0 Hz.
[e] $J_{C\text{-}6,F}$ = 34.2 Hz.
[f] $J_{C\text{-}4,F}$ = 21.7 Hz.
[g] $J_{C\text{-}5,F}$ = 238.0 Hz.
[h] $J_{C\text{-}6,F}$ = 34.0 Hz.

For NMR data, see Tables 1 and 2. Mass spectrum (LSIMS): $m/z$: 555.0040 [M$^+$+Na] for $C_{19}H_{18}N_2O_7FINa$ 555.0040. Anal. calcd for $C_{19}H_{18}N_2O_7FI$: C, 42.87; H, 3.41; N, 5.26. Found: C, 43.11; H, 3.65; N, 5.16%.

Compound **11**: (350 mg, 23%) solid foam; $[\alpha]_D^{25}$ −26.2 ($c$ 1.02); $\nu^{film}_{max}$ 3200, 3000, 1700 (C=O), and 1680 cm$^{-1}$. For NMR data, see Tables 1 and 2. Mass spectrum (LSIMS): $m/z$: 537.0503 [M$^+$+Na] for $C_{20}H_{23}N_2O_6INa$ 537.0498 (deviation −0.9 ppm). Anal. calcd for $C_{20}H_{23}N_2O_6I$: C, 46.70; H, 4.51; N, 5.44. Found: C, 46.99; H, 4.82; N, 5.51%.

Compound **12**: (320 mg, 21%) white crystals; mp 125–126°C (from ether–hexane); $[\alpha]_D^{24}$ −33.4 ($c$ 0.8); $\nu^{KBr}_{max}$ 3050, 2920, 1720 (C=O), and 1680 cm$^{-1}$. For NMR data, see Tables 1 and 2. Mass spectrum (LSIMS): $m/z$: 523.0331 [M$^+$+Na] for $C_{19}H_{21}N_2O_6INa$ 523.0342 (deviation +2.1 ppm). Anal. calcd for $C_{19}H_{21}N_2O_6I$: C, 45.62; H, 4.23; N, 5.60. Found: C, 45.89; H, 4.43; N, 5.58%.

Compound **13**: (950 mg, 61%) solid foam; $[\alpha]_D^{25}$ −43.6 ($c$ 1.1); $\nu^{film}_{max}$ 2020, 1720 (C=O), and 1700 cm$^{-1}$. For NMR data, see Tables 1 and 2. Mass spectrum (LSIMS): $m/z$: 541.0248 [M$^+$+Na] for $C_{19}H_{20}N_2O_6FINa$ 541.0248 (deviation −0.1 ppm). Anal. calcd for $C_{19}H_{20}N_2O_6I$: C, 44.03; H, 3.89; N, 5.40. Found: C, 44.29; H, 4.03; N, 5.42%.

Compound **14**: (1.03 g, 65%) solid foam; $[\alpha]_D^{25}$ +26.3 ($c$ 0.92); $\nu^{film}_{max}$ 1770 (C=O), 1710, and 1260 cm$^{-1}$. For NMR data, see Tables 3 and 4. Mass spectrum (LSIMS): $m/z$: 551.0287 [M$^+$+Na] for $C_{20}H_{21}N_2O_7INa$ 551.0291 (deviation +0.8 ppm). Anal. calcd for $C_{20}H_{21}N_2O_7I$: C, 45.47; H, 4.00; N, 5.30. Found: C, 45.82; H, 4.26; N, 5.44%.

Compound **15**: (1.315 g, 85%) solid foam; $[\alpha]_D^{24}$ +42.4 ($c$ 1.1); $\nu^{film}_{max}$ 2960, 1740 (C=O), 1690, and 1660 cm$^{-1}$. For NMR data, see Tables 3 and 4. Mass spectrum (LSIMS): $m/z$: 537.0128 [M$^+$+Na] for $C_{19}H_{19}N_2O_7INa$ 537.0135 (deviation +1.3 ppm). Anal. calcd for $C_{19}H_{19}N_2O_7I$: C, 44.37; H, 3.72; N, 5.44. Found: C, 44.21; H, 3.95; N, 5.50%.

Compound **16**: (1.393 g, 90%) white crystals; mp 165°C dec.; $[\alpha]_D^{27}$ +60.6 ($c$ 1); $\nu^{KBr}_{max}$ 3080, 1720 (C=O), and 1640 cm$^{-1}$. For NMR data, see Tables 3 and 4. Mass spectrum (LSIMS): $m/z$: 536.0290 [M$^+$+Na] for $C_{19}H_{20}N_3O_6INa$ 536.0294 (deviation +0.8 ppm). Anal. calcd for $C_{19}H_{20}N_3O_6I$: C, 44.37; H, 4.11; N, 8.17. Found: C, 44.29; H, 3.83; N, 8.09%.

Compound **17**: (1.065 g, 69%) solid foam; $[\alpha]_D^{24}$ −31 ($c$ 1.1); $\nu^{film}_{max}$ 3220, 3080, 1750 (C=O), and 1700 cm$^{-1}$. For NMR data, see Tables 3 and 4. Mass spectrum (LSIMS): $m/z$: 537.0498 [M$^+$+Na] for $C_{20}H_{23}N_2O_6INa$ 537.0498. Anal. calcd for $C_{20}H_{23}N_2O_6I$: C, 46.70; H, 4.51; N, 5.44. Found: C, 47.02; H, 4.68; N, 5.36%.

**Table 3.** $^1$H NMR chemical shifts ($\delta$) and $J$ (Hz) values for compounds **14**–**19**

| Compound | H-1′ | H-2′ | H-3′ | H-5′a | H-5′b | H-3 | H-5 | H-6 | $NH_2$ | Me | $CMe_2$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **14**[a] | 5.97d | 4.99dd | 5.85d | 4.40d | 3.89d | 9.29bs | – | 7.56s | – | 1.87s | 1.60 |
| | $J_{1',2'}$ 2.6 | $J_{2',3'}$ 4.9 | | $J_{5'a,5'b}$ 11.4 | | | | | | | 1.36 |
| **15**[b] | 5.98d | 5.03dd | 5.89d | 4.43d | 3.95d | 9.40bs | 5.68d | 7.76d | – | – | 1.64 |
| | $J_{1',2'}$ 2.7 | $J_{2',3'}$ 4.9 | | $J_{5'a,5'b}$ 11.5 | | | $J_{5,6}$ 8.2 | | | | 1.40 |
| **16**[a]* | 6.00d | 4.94dd | 5.74d | 4.52d | 3.84d | – | 5.73d | 7.37d | 7.20s | – | 1.47 |
| | $J_{1',2'}$ 3.1 | $J_{2',4'}$ 5.3 | | $J_{5'a,5'b}$ 11.0 | | | $J_{5,6}$ 7.7 | | | | 1.28 |
| **17**[a] | 5.72d | 4.53dd | 4.50d | 4.28d | 3.74d | 9.30bs | – | 7.51s | – | 1.94s | 1.60 |
| | $J_{1',2'}$ 2.8 | $J_{2',3'}$ 5.0 | | $J_{5'a,5'b}$ 11.8 | | | | | | | 1.39 |
| **18**[b] | 5.71d | 4.54dd | 4.50d | 4.29d | 3.76d | 9.50bs | 5.73d | 7.70d | – | – | 1.61 |
| | $J_{1',2'}$ 2.9 | $J_{2',3'}$ 5.0 | | $J_{5'a5'b}$ 11.8 | | | $J_{5,6}$ 8.4 | | | | 1.40 |
| **19**[a]* | 5.83d | 4.76dd | 4.53d | 4.47d | 3.53d | – | 5.70d | 7.67d | 7.16 | – | 1.46 |
| | $J_{1',2'}$ 3.0 | $J_{2',3'}$ 4.8 | | $J_{5'a,5'b}$ 11.0 | | | $J_{5,6}$ 7.6 | | | | 1.32 |

[a] Recorded at 400 MHz.
[b] Recorded at 300 MHz.
*Recorded in DMSO-$d_6$.

**Table 4.** $^{13}$C NMR chemical shifts ($\delta$) for compounds **8**–**13**

| Compound | C(2) | C(4) | C(5) | C(6) | C(1′) | C(2′) | C(3′) | C(4′) | C(5′) | Me |
|---|---|---|---|---|---|---|---|---|---|---|
| **14**[a] | 149.8 | 164.3 | 109.2 | 136.1 | 103.9 | 79.9 | 76.9 | 96.3 | 10.0 | 12.8 |
| **15**[b] | 149.8 | 165.0 | 100.9 | 140.3 | 103.9 | 79.9 | 76.7 | 96.5 | 10.1 | – |
| **16**[a]* | 154.7 | 166.1 | 93.0 | 141.4 | 104.0 | 79.8 | 76.5 | 95.8 | 11.5 | – |
| **17**[a] | 149.9 | 164.4 | 109.4 | 136.4 | 103.8 | 80.4 | 82.5 | 97.7 | 10.4 | 12.8 |
| **18**[b] | 149.9 | 163.9 | 101.1 | 138.9 | 103.8 | 80.4 | 82.5 | 98.0 | 10.5 | – |
| **19**[a]* | 154.7 | 166.0 | 92.9 | 141.4 | 103.5 | 80.2 | 82.4 | 96.8 | 12.0 | – |

[a] Recorded at 100 MHz.
[b] Recorded at 80 MHz.
*Recorded in DMSO-$d_6$.

Compound **18**: (620 mg, 41%) solid foam; $[\alpha]_D^{24}$ −21.6 (*c* 1); $\nu^{film}_{max}$ 3050, 1690 (C=O), and 1670 $cm^{-1}$. For NMR data, see Tables 3 and 4. Mass spectrum (LSIMS): *m*/*z*: 523.0340 [$M^+$+Na] for $C_{19}H_{21}N_2O_6INa$ 523.0342 (deviation +0.2 ppm). Anal. calcd for $C_{19}H_{21}N_2O_6I$: C, 45.62; H, 4.23; N, 5.60. Found: C, 45.82; H, 4.08; N, 5.71%.

Compound **19**: (1.424 g, 93%) white crystals; mp 132–133°C (from ether); $[\alpha]_D^{25}$ −32 (*c* 1.1, methanol); $\nu^{film}_{max}$ 2940, 1650 (C=O), and 1630 $cm^{-1}$. For NMR data, see Tables 3 and 4. Mass spectrum (LSIMS): *m*/*z*: 522.0501 [$M^+$+Na] for $C_{19}H_{22}N_3O_5INa$ 522.0502 (deviation +0.1 ppm). Anal. calcd for $C_{19}H_{22}N_3O_5I$: C, 45.70; H, 4.44; N, 8.41. Found: C, 45.52; H, 4.36; N, 8.39%.

Compound **20**: (350 mg, 23%) was also isolated as a syrup from the reaction of **7** with persilylated uracil and had $[\alpha]_D^{22}$ +32.5 (*c* 1.1); $\nu^{film}_{max}$ 2940, 1720 (C=O), and 1670 $cm^{-1}$. $^1$H NMR data: (400 MHz), 7.58 (d, 1H, $J_{5,6}$ = 8.4 Hz, H-6). 7.37–7.31 (m, 5H, Ph), 6.62 (d, 1H, $J_{1'',2''}$ = 6.5 Hz, H-1″), 5.62 (d, 1H, H-5), 5.57 (d, 1H, $J_{1',2'}$ = 2.9 Hz, H-1′), 5.00 (t, 1H, $J_{2'',3''}$ = 6.3 Hz, H-2″), 4.81–4.63 (m, 4H, 2$CH_2$Ph), 4.51 (t, 1H, $J_{2',3'}$ = 3.7 Hz, H-2′), 4.50 (d, 1H, H-3″), 4.42 (d, 1H, H-3′), 4.22 (d, 1H, $J_{5'a,5'b}$ = 11.7 Hz, H-5′a), 4.08 (d, 1H, $J_{5''a,5''b}$ = 10.9 Hz, H-5″a), 3.96 (d, 1H, H-5″b), 3.72 (d, 1H, H-5′b), 1.62, 1.59, 1.50 and 1.39 (4s, 12H, 2$CMe_2$); $^{13}$C NMR (100 MHz), 202.2 (C-4″), 162.6 (C-4), 149.5 (C-2), 139.0 (C-6), 137.5, 136.7, 128.6, 128.5, 128 4, 128.3, 128.2, and 128.1 (Ph), 116.1 and 111.8 (2*C*$Me_2$), 103.8 (C-5), 100.5 (C-1″), 98.2 (C-4′), 82.3, 81.9, 81.7, 81.2, and 75.8 (C-1″,2″,3″,2′,3′), 28.6, 27.8, 27.1 and 26.4 (2C*Me*$_2$), 10.3 (C-5′), 5.2 (C-5″). Mass spectrum (LSIMS): *m*/*z*: 911.0515 [$M^+$+Na] for $C_{34}H_{38}N_2O_{10}I_2Na$ 911.0514 (deviation −0.1 ppm).

### 3.8. Catalytic hydrogenation of 10

Compound **10** (50 mg, 0.09 mmol) in anhydrous methanol (15 mL) was hydrogenated at room temperature over 10% Pd–C at 4 atm for 2 h to afford crystalline **21** (38 mg, quantitative); mp 207–208°C (from ether–hexane); $[\alpha]_D^{22}$ +15 (*c* 1); $\nu^{KBr}_{max}$ 3070, 1730 (C=O), and 1670 $cm^{-1}$. $^1$H NMR data (inter alia): (400 MHz), 7.47 (d, 1H, $J_{6,F}$ = 5.7 Hz, H-6), 6.34 (dd, 1H, $J_{1',2'}$ = 6.4, $J_{1',F}$ = 1.5 Hz, H-1′), 5.80 (d, 1H, $J_{2',3'}$ = 4.0 Hz, H-3′), 4.54 (dd, 1H, H-2′), and 2.29 (s, 3H, Me*C*O); $^{13}$C NMR (100 MHz), 204.5 (Me*C*O), 165.3 (PhCO), 156.5 (d, $J_{C\text{-}4,F}$ = 26.9 Hz, C-4), 149.1 (C-2), 141.0 (d, $J_{C\text{-}5,F}$ = 238.7 Hz, C-5), 134.1, 130.0, 128.9, and 128.5 (Ph), 123.0 (d, $J_{C\text{-}6,F}$ = 34 Hz, C-6), 111.9 (*C*$Me_2$), 83.3 (C-1′), 79.4 and 76.0 (C-2′,3′), 28.0 (*Me*CO), 27.4 and 27.0 (C*Me*$_2$). Mass spectrum (LSIMS): *m*/*z*: 429.1078 [$M^+$+Na] for $C_{19}H_{19}N_2O_7FNa$ 429.1074 (deviation −0.9 ppm). Anal. calcd for $C_{19}H_{19}N_2O_7F$: C, 56.16; H, 4.71; N, 6.89. Found: C, 55.98; H, 5.00; N, 6.51%.

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