Synthesis of 2′,3′-Didehydro-2′,3′-dideoxyformycin A, 2′,3′-Dideoxyformycin A and 2′,3′-Dideoxytubercidin

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2′,3′-Didehydro-2′,3′-dideoxyformycin A **(7)** was prepared by reaction of the 7-amino-3-[5-*O*-(2-acetoxyisobutyryl)-3-bromo-3-deoxy-2-*O*-phenoxy(thiocarbonyl)-β-D-xylofuranosyl]-1*H*-pyrazolo[4,3-*d*]-pyrimidine **(5)** or 7-amino-3-[5-*O*-(2-acetoxyisobutyryl)-2-bromo-2-deoxy-3-*O*-phenoxy(thiocarbonyl)-β-D-arabinofuranosyl]-1*H*-pyrazolo[4,3-*d*]pyrimidine **(9)** with tributyltin hydride and subsequent deprotection of the resulting 5′-*O*-(2-acetoxyisobutyryl)-2′,3′-didehydro-2′,3′-dideoxyformycin A **(6)**. 2′,3′-Dideoxyformycin A **(13)** and 2′,3′-dideoxytubercidin **(16)** were synthesized via deoxygenation of their respective 3′-deoxy counterparts **10** and **2**, respectively.

The synthesis of 2′,3′-didehydro-2′,3′-dideoxy nucleosides and 2′,3′-dideoxynucleosides has become particularly important in connection with the anti HIV activity displayed by some of these compounds.[1] So far the methods used for the preparation of 2′,3′-unsaturated nucleosides included β-elimination of 2′-*O*-sulphonyl esters of 2′-deoxy nucleosides,[2] reductive elimination of 2′(3′)-acetoxy-3′(2′)-halo derivatives,[3,4] and other approaches.[5,6]

Although Barton-type deoxygenation[7] was widely applied to the preparation of 2′,3′-dideoxynucleosides from 2′-deoxynucleosides,[8] a free radical β-elimination[9] leading up to the 2′,3′-unsaturated systems was until recently not employed in nucleoside chemistry.[10,11] This report describes the preparation of 2′,3′-didehydro-2′3′-dideoxyformycin A via a free radical β-elimination of bromo- and phenoxy(thiocarbonyl) leaving groups, as well as the synthesis of 2′,3′-dideoxyformycin A and 2′,3′-dideoxytubercidin by hitherto undescribed deoxygenation of their respective 3′-deoxy counterparts previously prepared in our laboratory.[12,13]

The starting materials required for the synthesis, **4, 8** and **10**, were prepared by literature procedures.[12,14] Compound **2** was obtained by the reaction of 3′-deoxytubercidin **(1)**[13,14] with diphenyl (4-methoxyphenyl) methyl chloride (4-methoxytrityl chloride). Initial attempts at tritylation with 4-methoxytrityl chloride in pyridine afforded the expected 5′-*O*-(4-methoxytrityl)-3′-deoxytubercidin **(2)** in only 38 % yield. Subsequent use of silver nitrate as a catalyst and the mixture pyridine/tetrahydrofuran as a solvent[15,16] enabled an increase in the yield of the tritylation at the 5′-position to 72 % with only 5 % of the less polar *N*-4-(4-methoxytrityl)-3′-deoxytubercidin **(3)** being isolated.

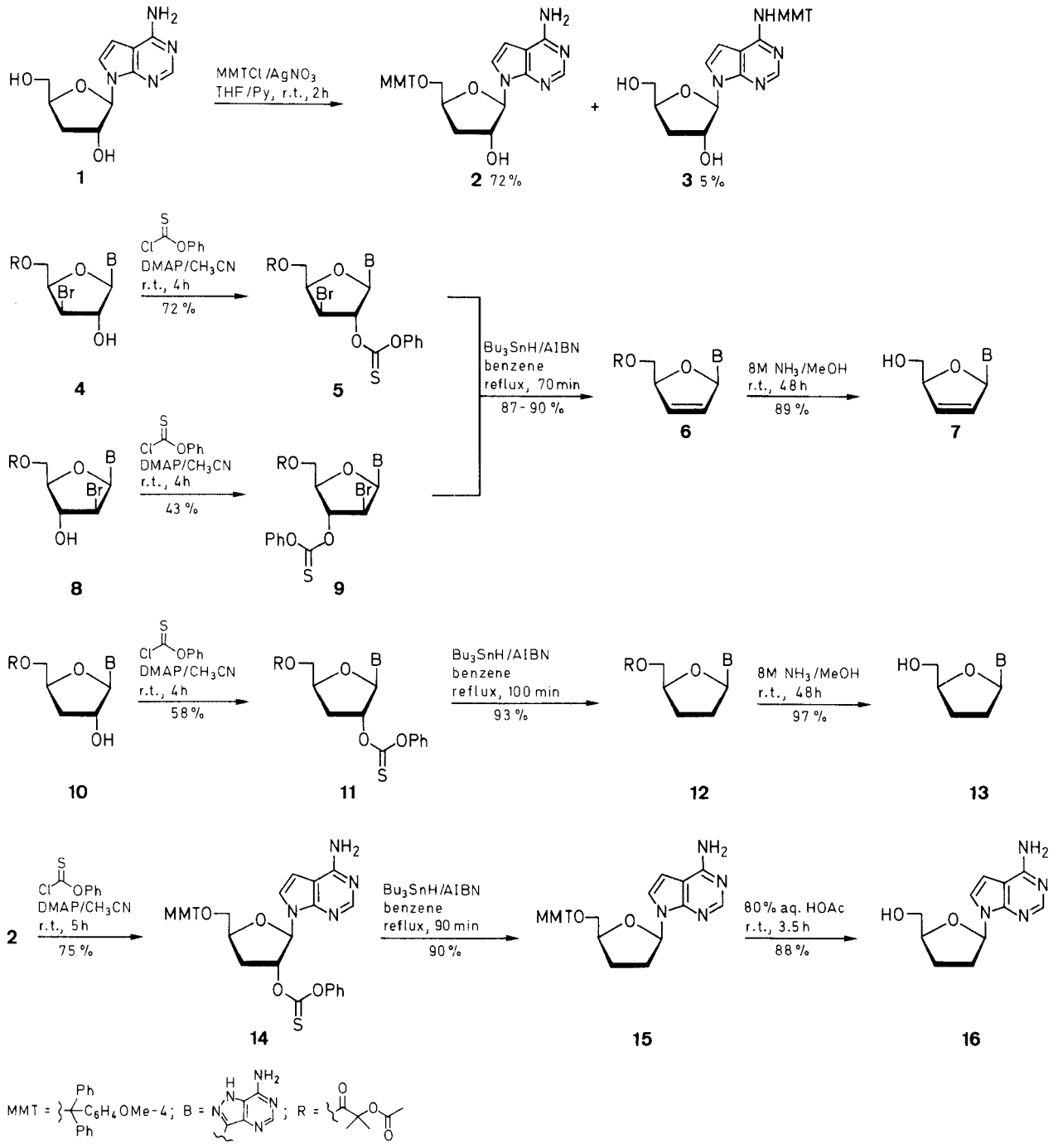
The synthetic route towards 2′,3′-didehydro-2′,3′-dideoxyformycin A **(7)** is outlined in the Scheme. 7-Amino-3-[5-*O*-(2-acetoxyisobutyryl)-3-bromo-3-deoxy-β-D-xylofuranosyl]-1*H*-pyrazolo[4,3-*d*] pyrimidine **(4)**[12,14] was acylated with *O*-phenylchlorothionoformate in the presence of dimethylaminopyridine[7] to give 7-amino-3-[5-*O*-(2-acetoxyisobutyryl)-3-bromo-3-deoxy-2-*O*-phenoxy (thiocarbonyl)]-1*H*-pyrazolo[4,3-*d*]-pyrimidine **(5)** in 72 % yield.

When **5** was allowed to react with tributyltin hydride in benzene in the presence of 2,2′-azobis(2-methylpropionitrile) (AIBN), the only product of the reaction, which could be conveniently isolated by column chromatography on silica gel in 87 % yield, was 5′-*O*-(2-acetoxyisobutyryl)-2′,3′-didehydro-2′,3′-dideoxyformycin A **(6)**. The formation of the 2′,3′-double bond was confirmed by the ^{1}H-NMR spectrum, which showed characteristic signals at $\delta = 6.07-6.18$ corresponding to the olefinic 2′ and 3′-protons. The quantitative removal of the 2-acetoxyisobutyryl group from **6** was achieved with 8 M methanolic ammonia; the resulting 2′,3′-didehydro-2′,3′-dideoxyformycin A **(7)** was homogeneous on HPLC and had spectroscopic data in agreement with those reported earlier.[3,17]

Compound **7** could also be obtained when 7-amino-3-[5-*O*-(2-acetoxyisobutyryl)-2-bromo-2-deoxy-β-D-arabinofuranosyl]-1*H*-pyrazolo[4,3-*d*]pyrimidine **(8)**[12,14] was used as the starting material. The acylation of **8** with *O*-phenylchlorothionoformate in the presence of dimethylaminopyridine was less selective than in the case of **4**. Examination of the reaction mixture by HPTLC revealed the presence of small amounts of side products with R_f values higher than that of **9**, which could derive from the acylation at both 2′ and *N*-7 positions. The expected 7-amino-3-[5-*O*-(2-acetoxyisobutyryl)-2-bromo-2-deoxy-3-*O*-phenoxy(thiocarbonyl)-β-D-arabinofuranosyl]-1*H*-pyrazolo[4,3-*d*]pyrimidine **(9)** was isolated in 43 % yield following column chromatography on silica gel.

The reaction of **9** with tributyltin hydride under conditions similar to those described for compound **5** afforded 5′-*O*-(2-acetoxyisobutyryl)-2′,3′-didehydro-2′3′-dideoxyformycin A **(6)** in virtually quantitative yield. It was also shown that the reaction of the mixture of the compounds **5** and **9** with tributyltin hydride affords exclusively the protected 2′,3′-didehydro-2′,3′-dideoxyformycin A **(6)** regardless of the ratio of **5** to **9**.

2′,3′-Dideoxyformycin A **(13)** was synthesized as follows. 5′-*O*-(2-Acetoxyisobutyryl)-3′-deoxyformycin A **(10)**[12,14] was allowed to react with *O*-phenylchlorothionoformate in the presence of dimethylaminopyridine to give 7-amino-3-[5-*O*-(2-acetoxyisobutyryl)-3-deoxy-2-*O*-phenoxy(thiocarbonyl)-β-D-ribofuranosyl]-1*H*-pyrazolo-[4,3-*d*]pyrimidine **(11)** in 58 % yield. Deoxygenation of **11** with tributyltin hydride in the presence of 2,2′-azobis-(2-methylpropionitrile) in benzene, afforded 5′-*O*-(2-acetoxyisobutyryl)-2′,3′-dideoxyformycin A **(12)**. Subsequent removal of the 5′-*O*-(2-acetoxyisobutyryl) group from **12** with 8 M methanolic ammonia afforded 2′,3′-dideoxyformycin A **(13)** in 90 % yield based on **11**. The structure of the nucleoside **13** was confirmed by crystallographic analysis of its hydrochloride[18] as well as by



spectroscopic data, which agreed with those quoted earlier.[14]

Compound **2** reacted with *O*-phenylchlorothionoformate in the presence of dimethylaminopyridine to give 4-amino-7-[-3-deoxy-5-*O*-4-methoxytrityl-2-*O*-phenoxy-(thiocarbonyl)-β-D-ribofuranosyl]-7*H*-pyrrolo[2,3-*d*]-pyrimidine **(14)**. The deoxygenation of **14** with tributyltin hydride in benzene in the presence of 2,2'-azobis-(2-methylpropionitrile) afforded the protected 2',3'-dideoxynucleoside **15**. The formation of the 2',3'-dideoxy system was clear from the ^{1}H-NMR spectrum which showed characteristic signals at $\delta = 2.07$ and 2.30 corresponding to the 2' and 3'-protons. Finally, the 4-methoxytrityl group was removed from **15** with 80% aqueous acetic acid to give the deprotected 2',3'-dideoxytubercidin **(16)** in nearly quantitative yield. The spectroscopic data of **16** agreed well with the literature values.[8,14,19,20]

The route outlined above has a great potential as a general way of creating the 2',3'-unsaturated system in nucleosides and other leaving groups such as 2,4,6-trichlorophenoxy(thiocarbonyl) and pentafluorophenoxy (thiocarbonyl)[21] are being investigated.

Melting points were determined on a Reichert micro hot stage apparatus and are uncorrected. UV spectra were measured in 95% EtOH with a Pye-Unicam SP-8-150 UV-Vis spectrometer. ^{1}H-NMR spectra were recorded at 250 MHz with a Bruker WH 250 spectrometer with TMS as an internal standard and DMSO-d_6 as a solvent. In cases where analytical data are given for hydrates the presence of water was confirmed by means of ^{1}H-NMR; the protons of 2'-OH, 3'-OH, NH_2, NH and H_2O were exchangeable with D_2O.

Table 1. Compounds **5**, **9**, **11** and **14** Prepared

Product[a]	Yield (%)	Molecular Formula[b]	R_f: Solvent Systems A, B, C	UV (95% EtOH) λ_{max} (nm) (log ε), λ_{min} (nm) (log ε)	^{1}H-NMR (DMSO-d_6/TMS) δ, J(Hz)
5	72	$C_{23}H_{24}BrN_5O_7S$ (562.4)	0.12, 0.38, 0.66	293 (4.02), 263 (3.74)	1.48, 1.53 [2s, 6H, $(CH_3)_2C$], 3.35 (s, H_2O), 4.19, 4.43 (2m, 3H, H-5'a, H-5'b, H-4'), 5.05 (m, 1H, H-3'), 5.47 (d, 1H, J = 4.01, H-1'), 6.64 (d, 1H, J = 3.29, H-2'), 7.36 (m, 7H, $C_6H_5 + NH_2$), 8.19, 8.22 (2s, 1H, H-5), 12.85, 13.00 (2 br s, 1H, NH)
9	43	$C_{23}H_{24}BrN_5O_7S$ (562.4)	0.12, 0.38, 0.66	294 (4.02), 263 (3.70)	1.51 [s, 6H, $(CH_3)_2C$], 2.02 (s, 3H, CH_3CO), 4.46 (m, 3H, H-4', H-5'a, H-5'b), 5.26 (s, 1H, H-2'), 5.66 (d, 1H, J = 4.8, H-1'), 6.16 (s, 1H, H-3'), 7.30 (m, 7H, $C_6H_5 + NH_2$), 8.20 (s, 1H, H-5), 12.83 (br s, 1H, NH)
11	58	$C_{23}H_{25}N_5O_7S$ (515.5)	0.06, 0.27, 0.62	294 (4.00), 264 (3.72)	1.37, 1.39 [2s, 6H, $(CH_3)_2C$], 1.95, 1.96 (2s, 3H, CH_3CO), 2.38, 2.68 (2m, 2H, H-3'a, H-3'b), 3.39 (s, H_2O), 4.13, 4.28 (2m, 2H, H-5'a, H-5'b), 4.40 (m, 1H, H-4'), 5.32 (d, 0.6H, J = 1.94), 5.47 (d, 0.4H, J = < 1, H-1'), 6.12, 6.20 (2m, 1H, H-2'), 7.45 (m, 7H, $C_6H_5 + NH_2$), 8.20, 8.32 (2s, 1H, H-5), 12.88 (br s, 1H, NH)
14	75	$C_{38}H_{34}N_4O_5S$ (658.8)	0.20, 0.48, 0.77	270 (4.13), 249 (3.95)	2.42 (m, 1H, H-3'a), 2.87 (m, 1H, H-3'b), 3.20 (m, 2H, H-5'a, H-5'b), 3.73 (s, 3H, OCH_3), 4.47 (m, 1H, H-4'), 6.14 (1H, d, J = 5.7, H-1'), 6.44 (d, 1H, J = < 1, H-2'), 6.58 (d, 1H, J = 3.52, H-5), 6.82 (d, $2H_{arom}$, J = 8.75), 7.32 (m, 18H, $17H_{arom}$ + H-6), 8.08 (s, 1H, H-2)

[a] The products were obtained as amorphous powders having indefinite melting points.
[b] Satisfactory microanalyses obtained: C ±0.26, H ±0.21, N ±0.36.

Table 2. Compounds **6**, **12** and **15** Prepared

Product[a]	Yield (%)	Molecular Formula[b]	R_f: Solvent Systems A, B, C	UV (95% EtOH) λ_{max} (nm) (log ε), λ_{min} (nm) (log ε)	^{1}H-NMR (DMSO-d_6/TMS) δ, J(Hz)
6	87[c] 90[d]	$C_{16}H_{19}N_5O_5$ (361.3)	0.06, 0.20, 0.51	294 (3.96), 247 (3.55)	1.41, 1.42 [2s, 6H, $(CH_3)_2C$], 1.97 (s, 3H, CH_3CO), 3.36 (s, H_2O), 4.30 (m, 2H, H-5'a, H-5'b), 4.97 (m, 1H, H-4'), 6.07–6.18 (m, 3H, H-1', H-2', H-3'), 7.30 (br s, 2H, NH_2), 8.17 (s, 1H, H-5), 12.80 (br s, 1H, NH)
12	93	$C_{16}H_{21}N_5O_5$ (363.4)	0.06, 0.20, 0.52	294 (4.00), 264 (3.72)	1.43, 1.45 [2s, 6H, $(CH_3)_2C$], 1.97 (s, 3H, $COCH_3$), 2.08, 2.54 (2m, 4H, H-2'a, b, H-3'a, b), 3.32 (s, H_2O), 4.17 (m, 3H, H-4', H-5'a, H-5'b), 5.22 (pseudo t, 1H, J = 7.1, H-1'), 7.25 (br s, 2H, NH_2), 8.16 (s, 1H, H-5), 12.72 (br s, 1H, NH)
15	90	$C_{31}H_{30}N_4O_3$ (506.6)	0.15, 0.41, 0.68	273 (4.03), 250 (3.83)	2.07 (m, 2H, H-3'a, H-3'b), 2.26 (m, 1H, H-2'a), 2.34 (m, 1H, H-2'b), 3.15 (m, 2H, H-5'a, H-5'b), 3.32 (s, H_2O), 3.73 (s, 3H, OCH_3), 4.20 (m, 1H, H-4'), 6.43 (m, 1H, H-1'), 6.53 (d, 1H, J = 3.58, H-5), 6.82 (d, $2H_{arom}$, J = 8.92), 7.24 (m, 13H, $12H_{arom}$ + H-6), 8.06 (s, 1H, H-2)

[a] The products were obtained as amorphous powders having indefinite melting points.
[b] Satisfactory microanalyses obtained: C ±0.10, H ±0.19, N ±0.28.
[c] From **5**.
[d] From **9**.

HPLC analysis was performed on the system comprising Waters model 510 pump, model 680 automated gradient controller, model 46K injector and model 490 programmable wavelength detector. Retention times were determined on a Trilab 3000 multichannel chromatography data system (Trivector). The column – 5 μm APEX ODS 250 × 4.6 mm, Jones chromatography U.K., was eluted with different ratios of 0.025 M NH_4OAc buffer/CH_3CN under isocratic conditions. HPTLC was run on Merck silica gel 60 F_{254} analytical plates in the following solvent systems: (A) $CHCl_3$/EtOH (19:1), (B) $CHCl_3$/EtOH (9:1) and (C) $CHCl_3$/EtOH (4:1).

otherwise indicated. Formycin A monohydrate and tubercidin were purchased from Sigma whereas *O*-phenylchlorothionoformate, dimethylaminopyridine and tributyltin hydride from Aldrich.

4-Amino-7-[3-deoxy-5-*O*-(4-methoxytrityl)-β-D-ribofuranosyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine (2) and 4-(4-Methoxytrityl)amino-7-(3-deoxy-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (3): 3'-Deoxytubercidin[13,14] (**1**; 1.45 g, 5.8 mmol) is dissolved in THF (70 mL) and pyridine (21 mL). To the resulting pale pink solution, $AgNO_3$ (1.18 g, 7.0 mmol) is added in one portion and the suspension is warmed on an oil bath until the $AgNO_3$ dissolves. After

after the addition and the suspension is stirred at r.t. for further 2.5 h. The precipitate is filtered, washed with $CHCl_3$ and the combined filtrate and washings are concentrated under reduced pressure. The residue is partitioned between 5% aq $NaHCO_3$/$CHCl_3$ (4:1, 250 mL) and the aqueous layer is extracted with $CHCl_3$ (4 × 50 mL). The combined $CHCl_3$ extracts are washed with water (40 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The residue is applied to a short column of silica gel. Elution of the column with $CHCl_3$/EtOH (24:1) affords **3** as a colourless froth; yield: 0.16 g (5%). An analytical sample is obtained by precipitating a $CHCl_3$ solution of **3** with light petroleum (bp 30–40°C) and collecting the product by centrifugation; R_f = 0.16 (A), 0.47 (B), 0.73 (C).

3:

$C_{31}H_{30}N_4O_4.0.75\ H_2O$	calc.	C 69.45	H 5.92	N 10.45
(536.1)	found	69.88	5.86	10.58

UV: λ_{max} = 284 nm (log ε = 4.23), λ_{min} = 252 nm (log ε = 3.82).

^{1}H-NMR: δ = 1.89 (m, 1 H, H-3'a), 2.17 (m, 1 H, H-3'b), 3.35 (s, H_2O), 3.48 (m, 1 H, H-5'a), 3.58 (m, 1 H, H-5'b), 3.70 (s, 3 H, OCH_3), 4.25 (m, 1 H, H-4'), 4.39 (m, 1 H, H-2'), 5.03 (t, 1 H, J = 5.46 Hz, 5'-OH), 5.50 (d, 1 H, J = 4.38 Hz, 2'-OH), 5.97 (d, 1 H, J = 2.71 Hz, H-1'), 6.81 (d, 2 H_{arom}, J = 8.88 Hz), 6.96 (d, 1 H, J = 3.58 Hz, H-5), 7.25 (m, 13 H, 12 H_{arom} + H-6), 7.75 (s, 1 H, H-2), 7.99 (s, 1 H, NH).

Further elution with $CHCl_3$/EtOH (19:1) affords **2** as a colourless froth; yield: 2.25 g (72%). An analytical sample is obtained by precipitation from $CHCl_3$ as described for **3**; R_f = 0.09 (A), 0.35 (B), 0.61 (C).

2:

$C_{31}H_{30}N_4O_4.0.75\ H_2O$	calc.	C 69.45	H 5.92	N 10.45
(536.1)	found	69.28	5.82	10.37

UV: λ_{max} = 273 nm (log ε = 4.03), λ_{min} = 250 nm (log ε = 3.84).

^{1}H-NMR: δ = 1.94 (m, 1 H, H-3'a), 2.25 (m, 1 H, H-3'b), 3.17 (m, 2 H, H-5'a, H-5'b), 3.34 (s, H_2O), 3.73 (s, 3 H, OCH_3), 4.46 (m, 1 H, H-4'), 5.61 (d, 1 H, J = 4.02 Hz, 2'-OH), 6.10 (d, 1 H, J = < 1 Hz, H-1'), 6.52 (d, 1 H, J = 3.57 Hz, H-5), 6.85 (d, 2 H_{arom}, J = 8.82 Hz), 7.01 (br s, 2 H, NH_2), 7.25 (m, 13 H, 12 H_{arom} + H-6), 8.07 (s, 1 H, H-2).

Acylation of the Nucleosides 2, 4, 8 and 10 with *O*-Phenylchlorothionoformate; General Procedure:

To a stirred suspension of the nucleoside **2, 4, 8**, or **10**[12,14] (1 mmol) and dimethylaminopyridine (2 mmol or 1.5 mmol for **10**) in anhydrous CH_3CN (11 mL) a solution of *O*-phenylchlorothionoformate (1.5 mmol or 1.2 mmol for **10**) in anhydrous CH_3CN (5 mmol) is added in one portion. The resulting pale yellow, later orange solution is stirred at r.t. for 4 h or 5 h for 2. The solvent is removed under reduced pressure and the residue partitioned between EtOAc/water (4:1, 100 mL). The organic phase is washed with cold M HCl (2 × 20 mL) for **4**, **8**, **10**, water (20 mL), 5% $NaHCO_3$ (20 mL) water (20 mL) and dried (Na_2SO_4). The solvent is removed under reduced pressure and the residue is applied to a short column of silica gel. The product is eluted with $CHCl_3$/EtOH (24:1 for **4, 8** and **10** and 99:1 for **2**). The fractions containing the product are combined and concentrated under reduced pressure. Each colourless residue is dissolved in chloroform (~ 1 mL) and added dropwise to a stirred light petroleum (bp 30–40°C) (60 mL). The resulting colourless precipitate is collected by centrifugation and dried in a desiccator (Table 1).

Reaction of Phenoxy(thiocarbonyl) Nucleosides 5, 9, 11 and 14 with Tributyltin Hydride, General Procedure:

To a solution of the nucleoside **5, 9, 11** or **14** (1 mmol) in benzene (40 mL) tributyltin hydride (1.1 mL, 4 mmol for **5, 9** or 0.55 mL, 2 mmol for **11, 14**) and 2,2'-azobis (2-mehylpropionitrile) (AIBN, 0.050 g, 0.025 mmol) are added. The stirred reactants are heated under reflux for 70 min (**5, 9**), 100 min (**11**) or 80 min (**14**). The solvent is removed under reduced pressure and the residue is applied to a short column of silica gel. The product is eluted with $CHCl_3$/EtOH (47:3 for **6**, 24:1 for **12** and 97:3 for **15**). The fractions containing the product are combined and concentrated under reduced pressure. Each colourless residue is dissolved in $CHCl_3$ (~ 1 mL) and added dropwise to a stirred light petroleum (bp 30–40°C, 60–70 mL). The resulting colourless precipitate is collected by centrifugation and dried in a desiccator (Table 2).

7-Amino-3-(2,3-dideoxy-β-D-glyceropent-2-enofuranosyl)-1*H*-pyrazolo[4,3-*d*]pyrimidine (2',3'-Didehydro-2',3'-dideoxyformycin A, 7)

5'-*O*-(2-Acetoxyisobutyryl)-2',3'-didehydro-2',3'-dideoxyformycin A (**6**; 0.35 g, 1 mmol) is dissolved in 8 M methanolic ammonia (25 mL) and the solution is stirred at r.t. for 49 h. The solvent is removed under vacuo and the residue partitioned between water and $CHCl_3$ (4:1) (200 mL). The aqueous layer is extracted with $CHCl_3$ (5 × 20 mL) and Et_2O (25 mL), concentrated to a small volume and lyophilised to afford **7** as an amorphous colourless powder homogenous on HPLC; yield: 0.21 g (89%); R_f = 0.10 (B); retention time = 137 sec (0.025 NH_4OAc buffer/CH_3CN (80:20). The nucleoside is converted into its hydrochloride and is crystallised from EtOH to give small needles; mp 194–195°C (Lit.[3] mp 193°C); ^{1}H-NMR data agree with the literature[3] values.

UV: λ_{max} = 294 nm (log ε = 3.96); λ_{min} = 248 nm (log ε = 3.68).

7-Amino-3-(2,3-dideoxy-β-D-glyceropentofuranosyl)-1*H*-pyrazolo-[4,3-*d*]pyrimidine (2',3'-Dideoxyformycin A, 13):

5'-*O*-(2-Acetoxyisobutyryl)-2',3'-dideoxyformycin A (**12**; 0.36 g, 1 mmol) is deprotected following the procedure identical to that described for compound **6**. Lyophilisation affords **13** as an amorphous colourless powder homogeneous on HPLC; yield: 0.22 g (91%); R_f = 0.11 (B). The nucleoside is converted into its hydrochloride and is crystallised from EtOH to give small needles; mp 185–187°C (Lit.[14] mp 182–185°C); retention time = 267 sec (0.025 M (NH_4OAc/CH_3CN, 88:12) ^{1}H-NMR data agree with the literature values.[14]

UV: λ_{max} = 294 nm (log ε = 4.01), λ_{min} = 255 nm (log ε = 3.62).

4-Amino-7-(2,3-dideoxy-β-D-glyceropentofuranosyl)-7*H*-pyrrolo-[2,3-*d*]pyrimidine (2',3'-dideoxytubercidin, 16):

5'-*O*-(4-Methoxytrityl)-2',3'-dideoxytuberdicin **15**; 0.51 g, 1 mmol) is dissolved in 80% HOAc (25 mL) and the solution is stirred at r.t. for 3 h 15 min. The solvent is removed and the residue is coevaporated with toluene (3 × 15 mL) and partitioned between water/$CHCl_3$ (4:1, 250 mL). The aqueous layer is extracted with $CHCl_3$ (5 × 25 mL) and Et_2O (30 mL), concentrated to a small volume and lyophilised to give **1b** as an amorphous colourless powder homogeneous on HPLC; yield: 0.21 g (88%); R_f = 0.13 (B), 0.33 (C); retention time = 164 sec (0.025 M NH_4OAc/CH_3CN, 80:20). ^{1}H-NMR data agree with the literature[8,14,19,20] values.

UV: λ_{max} = 271 nm (log ε = 4.00); λ_{min} = 241 nm (log ε = 3.40).

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