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An Efficient Synthesis of 2'-*O*-(β-D-Ribofuranosyl)biopterin

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Abstract

N^2-(*N*,*N*-Dimethylaminomethylene)-3-[2-(4-nitrophenyl)ethyl]-1',2'-di-*O*-(trimethylsilyl)biopterin (**4**) was prepared from biopterin (**1a**, 86% overall yield) in 5 steps. Glycosylation of **4** with 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranose (**5a**) and its 2,3,5-tri-*O*-benzoyl analog (**5b**) respectively afforded the corresponding 2'-*O*-(2,3,5-tri-*O*-acetyl- and 2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)biopterin derivatives (**6a**, 42% and **6b**, 60%) as major products. Removal of the protecting groups of **6b** provided 2'-*O*-(β-D-ribofuranosyl)biopterin (**1c**, 87% overall yield) in 3 steps.

Key words: biopterin D-riboside, pterin glycoside, glycosylation, protecting groups

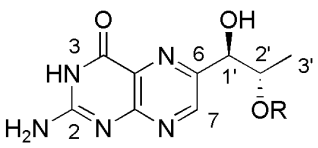
Introduction

Certain pterin glycosides carrying various kinds of sugars attached to the side-chain at C-6 of the pteridine ring were found to be produced by some prokaryotes as exemplified by glycosides of biopterin (**1a**): 2'-*O*-(β-D-glucopyranosyl)biopterin (**1b**) isolated from cyanobacteria (1-6) and 2'-*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)biopterin from anaerobic photosynthetic bacteria (7). Glycosides of L-*threo*-biopterin and 6-hydroxymethylpterin were also isolated from green sulfur bacteria and cyanobacteria (8-10). Some of these structures have been confirmed also by chemical syntheses (11-16).

As for biopterin D-riboside, 2'-*O*-(β-D-ribofuranosyl)biopterin (**1c**) found in *Spirulina platensis* (17) appears to be the only clear account to our knowledge. The structure was confirmed by comparison with the synthesized specimen **1c** obtained by the sequence illustrated in Scheme 1 (18). The overall yield of **1c** from **1a**, however, remained rather low (11%) and often fluctuated apparently due to the liability of the tetrakis-N^2,O^4,$O^{1'}$,$O^{2'}$-trimethylsilylated **1a** under the glycosylation conditions employed, thus mostly regenerating **1a**.

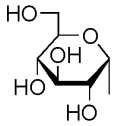
Since various types of glycosides of biopterin and

Formulae 1a-c

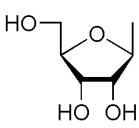


1a R = H (biopterin)

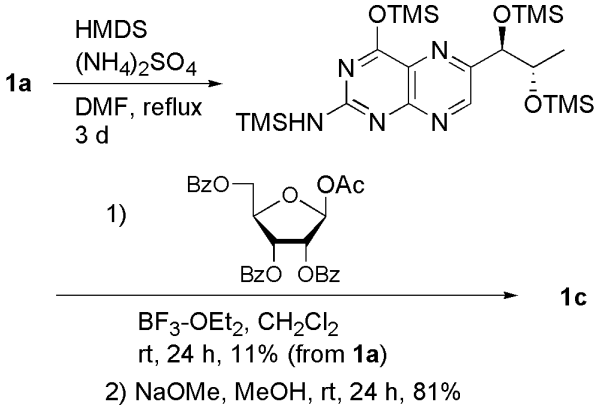
1b R =



1c R =



Scheme 1



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related pterins were considered to be of interest in view of their biological activities and functions, we have undertaken to explore more efficient glycosylations of biopterin leading to 2'-*O*-(β-D-ribofuranosyl)biopterin (**1c**).

Results and Discussion

Due to the effectively stabilized intramolecular hydrogen bondings in the solid state (19), pterin derivatives including biopterin are little soluble in nonpolar aprotic solvents in which glycosylation reactions normally proceed smoothly. Thus, biopterin (**1a**) was converted in a four step procedure via the intermediate 1',2'-di-*O*-acetyl-N^2-(*N*,*N*-dimethylaminomethylene) biopterin (**2**) (12,20) into the sufficiently solubilized and versatile N^2-(*N*,*N*-dimethylaminomethylene)-3-[2-(4-nitrophenyl)ethyl]biopterin (**3**) in 87% overall yield (Scheme 2). For the purpose of further raising the solubility of compound **3** in dichloromethane, **3** was silylated with 1,1,1,3,3,3-hexamethyldisilazane (HMDS) in the presence of ammonium sulfate in dichloromethane under reflux for 24 h, yielding the 1',2'-di-*O*-trimethylsilyl derivative (**4**) quantitatively.

Glycosylations of **4** with glycosyl donors, such as 1,2,3,5-tetra-*O*-acetyl- (**5a**) and 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (**5b**), was investigated under various conditions in the presence of an activator. Thus, treatment of **4** with 1.5-3.0 mol equiv. of **5a** or **5b** in the presence of tin(IV) chloride (2.0-4.0 mol equiv.) in dichloromethane at room temperature for 18-24 h afforded a mixture of fully protected 2'-*O*-(β-D-ribofuranosyl)biopterin (**6a,b**), 1'-*O*-(β-D-ribofuranosyl) isomer (**7a,b**), and 1',2'-di-*O*-(β-D-ribofuranosyl) derivatives (**8a,b**). The yields of these products depended upon the molar ratio of **4** to glycosyl donors as summarized in Table 1.

Although the mono- and di-glycosyl compounds were chromatographically separable on a silica gel column, separation of the monoglycosides **6a** and **7a** has not been achieved. Among entries 1-4, use of 1.5 mol equiv. of **5a** (Entry 2) gave monoglycosides (**6a, 7a**) in the highest yields with a moderate preference of 2'-*O*-glycosylation; 2'-*O*-glycoside:1'-*O*-glycoside = 78:22. Similar treatment of **4** with 2.0 mol equiv. of **5b** (Entries 5-8), however, afforded the best yield (60%) of 2'-*O*-monoglycoside (**6b**) along with a minor proportion (18% yield) of the 1',2'-di-*O*-glycoside (**8b**) (Entry 7). In the fraction of **6b**, a trace amount of a byproduct presumed to be the 1'-*O*-glycoside (**7b**) was detectable (by ^{1}H NMR); this byproduct was removable by recrystallization to provide pure **6b**. The higher preference of 2'-*O*-glycoside production from **5b** is

Scheme 2

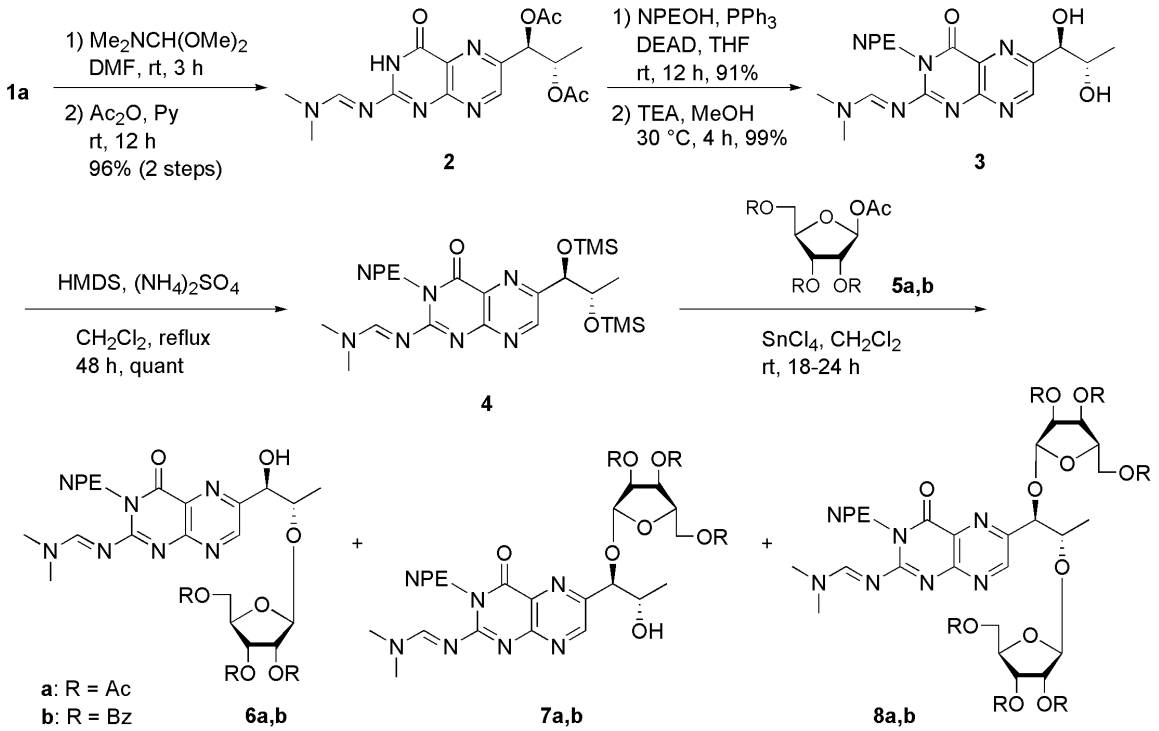


Table 1. Glycosylation of biopterin derivative (**4**)[a]

Entry	Glycosyl donor (mol equiv.)	Activator (mol equiv.)	Products (yield)[b]		
1	**5a** (1.5)	$SnCl_4$ (2.0)	**6a** (33%)	**7a** (9%)	**8a** (18%)
2	**5a** (1.5)	$SnCl_4$ (4.0)	**6a** (42%)	**7a** (12%)	**8a** (25%)
3	**5a** (2.0)	$SnCl_4$ (4.0)	**6a** (34%)	**7a** (7%)	**8a** (35%)
4	**5a** (2.5)	$SnCl_4$ (4.0)	**6a** (18%)	**7a** (3%)	**8a** (46%)
5	**5b** (1.5)	$SnCl_4$ (2.0)	**6b** (25%)	**7b** (<1%)	**8b** (11%)
6	**5b** (2.0)	$SnCl_4$ (2.0)	**6b** (48%)	**7b** (<1%)	**8b** (15%)
7	**5b** (2.0)	$SnCl_4$ (4.0)	**6b** (60%)	**7b** (<1%)	**8b** (18%)
8	**5b** (3.0)	$SnCl_4$ (4.0)	**6b** (19%)	**7b** (<1%)	**8b** (48%)

[a] All reactions were carried out in CH_2Cl_2 at rt for 18-24 h. [b] Yields of inseparable monoglycosides (**6a**) and (**7a**) were estimated by ^{1}H NMR spectra.

most likely ascribed to the presence of the bulkier protecting groups in the glycosyl donor (**5b**) compared to **5a**.

The assignment of the 1'-*O*-substituted structure of **7a** was derived from the doublet of the H-1' signal, whereas pseudotriplets of the H-1' for 2'-*O*-substituted compounds **6a,b** indicated the presence of a free 1'-OH group (Table 2). All D-ribofuranosyl moieties of these compounds possess a β-configuration at their glycosidic linkage due to their $J_{1,2}$ values (0.9-1.5 Hz). The stereoselective β-glycoside formation of all these products (**6-8a,b**) was attained mainly by participation of the neighboring groups (2-*O*-acetyl of **5a** and 2-*O*-benzoyl of **5b**). Although the H-1 signal of the 2'-*O*-glycoside (**6a**) appears at lower field compared with that of 1'-*O*-glycoside (**7a**), all other sugar protons of **6a** appear at upper field than those of **7a**. Such tendency is observed in both glycosyl moieties of 1',2'-di-*O*-glycosides (**8a,b**).

Removal of the protecting groups of the purified 2'-*O*-(tri-*O*-benzoyl-β-D-ribofuranosyl)biopterin derivative (**6b**) was performed according to the following three-step-procedures (Scheme 3): benzoyl groups of **6b** were cleaved by the treatment with sodium methoxide in methanol to afford **9**, which was then treated with aqueous ammonia-methanol to remove the *N*,*N*-dimethylaminomethylene group, followed by the action of DBU in DMF to cleave the NPE group, thus affording 2'-*O*-(β-D-ribofuranosyl)biopterin (**1c**) in 87% overall yield from **6b**. Structure of **1c** was unambiguously established as the corresponding pentaacetyl derivative (**11**) obtained by usual acetylation (Table 2). Treatment of **11** with aqueous ammonia regenerated **1c** quantitatively. The spectral data of **1c** (see Experimental part) were identical in all respects with those of the natural product (17,18).

An attempt to remove the NPE group of **6b** first by treatment with DBU for 24 h resulted in partial deprotection to give **10** in 46% yield and 31% recovery of **6b**. Compound **10** was then converted into **1c** by methanolysis of the benzoyl groups and the subsequent cleavage of *N*,*N*-dimethylaminomethylene group with aqueous ammonia. From these results, removal of the N^2-(*N*,*N*-dimethylaminomethylene) group prior to deprotection of *N*(3)-NPE was shown to be more effective.

An inseparable mixture of 2'-*O*- and 1'-*O*-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl) derivatives (**6a,7a**) was also subjected to similar deprotection steps described above to give the 2'-*O*- (**1c**) and 1'-*O*-(β-D-ribofuranosyl) isomers (**1d**) (Scheme 3). Although these compounds were converted into the pentaacetyl derivatives (**11, 12**), their separation could not be achieved.

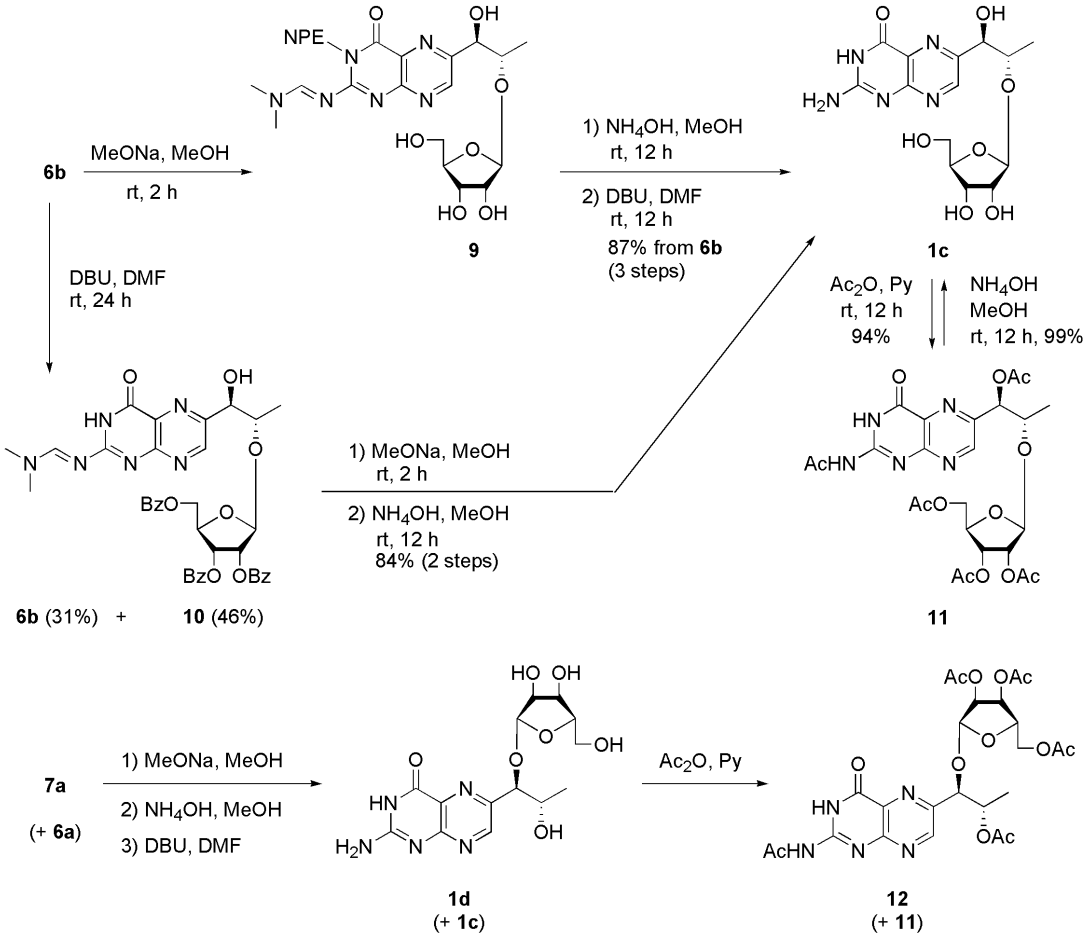
The present work thus demonstrates an effective way for the preparation of 2'-*O*-(β-D-ribofuranosyl) biopterin (**1c**). Improvements of selectivity for 2'-*O*-monoglycosylation as well as preparation of biopterin glycosides having various types of other sugar moieties are in progress.

Experimental

General procedures

All reactions were monitored by TLC (Merck silica gel 60F, 0.25 mm) with an appropriate solvent system [(*A*) 1:9 MeOH-$CHCl_3$ and (*B*) 5:3:1 2-PrOH-AcOEt-H_2O]. Column chromatography was performed with Daiso Silica Gel IR-60/210w. Components were detected by exposing the plates to UV light and/or spraying them with 20% sulfuric acid-ethanol (with subsequent heating). The NMR spectra were measured in $CDCl_3$ or DMSO-d_6 with Varian Unity Inova AS600 (600 MHz) spectrometers at 23°C. Chemical shifts are reported as values relative to a solvent peak (7.26 ppm for $CDCl_3$, 2.50 ppm for DMSO-d_6) as an internal standard.

Scheme 3



N^2-(N,N-Dimethylaminomethylene)-3-[2-(4-nitrophenyl)ethyl]-1',2'-di-O-(trimethylsilyl)biopterin (**4**) (12)

According to the reported procedures (12,20), compound **3** was prepared from biopterin in 4 steps. A suspension of **3** (550 mg, 1.25 mmol), ammonium sulfate (400 mg, 3.03 mmol), and HMDS (3.00 mL, 14.5 mmol) in dry CH_2Cl_2 (30 mL) was refluxed for 24 h. The precipitate was filtered off and the filtrate was evaporated in vacuo. The residue was purified by short-path column chromatography with 2% MeOH-$CHCl_3$ to give **4** (722 mg, 99%) as a pale yellow foam: R_f 0.65 (*A*).

N^2-(N,N-Dimethylaminomethylene)-3-[2-(4-nitrophenyl)ethyl]-2'-O-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)biopterin (**6a**)*, its 1'-O-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl) isomer* (**7a**)*, and N^2-(N,N-dimethylaminomethylene)-3-[2-(4-nitrophenyl)ethyl]-1',2'-bis-O-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)biopterin* (**8a**)

To a solution of **5a** (200 mg, 0.628 mmol) in CH_2Cl_2 (4.0 mL) was added $SnCl_4$ (0.19 mL, 1.67 mmol) at 0°C. After stirring at 0°C for 0.5 h, a solution of **4** (240 mg, 0.410 mmol) in CH_2Cl_2 (3.0 mL) was added and then the mixture was stirred at rt for 20 h. After addition of saturated aqueous $NaHCO_3$, the mixture was extracted with $CHCl_3$. The organic layer was dried (Na_2SO_4) and evaporated in vacuo. The residue was separated by column chromatography with 1:2 AcOEt-hexane and then 2% MeOH-$CHCl_3$ into two fractions.

The faster-eluting fraction [R_f 0.55 (*A*)] gave **8a** (98.0 mg, 25%) as a pale yellow powder: mp 82-84°C (from AcOEt-hexane); ^{1}H NMR, see Table 2. Anal. calc. for $C_{42}H_{51}N_7O_{19}$ (957.89): C52.66, H5.37; found: C52.42, H5.44.

The slower-eluting fraction [R_f 0.48 (*A*)] gave a pale yellow powder (155 mg), which consisted of **6a** (120 mg, 42%) and **7a** (35 mg, 12%), the ratio being estimated by ^{1}H NMR spectrum: ^{1}H NMR for **6a** and **7a**, see Table 2. Anal. calc. for $C_{31}H_{37}N_7O_{12}$ (699.67): C53.22, H5.33; found: C53.36, H5.18.

Table 2. 600 MHz ^{1}H-NMR Spectral parameters for 1'- and 2'-*O*-(β-D-ribofuranosyl)biopterin derivatives (**6-8a,b, 11, 12**) in $CDCl_3$

	Chemical shifts / δ (coupling constants / Hz)										
	Biopterin moiety				Me_2NCH=N-2		NPE-N(3)				
Compound	H-7	H-1' ($J_{1',2'}$)	H-2' ($J_{2',3'}$)	H_3-3'	Me_2N	CH=N	H(*o*) ($J_{o,m}$)	H(*m*)	CH_2CH_2N ($^3J_{H,H}$)	CH_2N ($^2J_{H,H}$)	Other signals
6a	8.92	4.99 (4.6)	4.20 (6.6)	1.20	3.24, 3.19	8.88	7.42 (8.8)	8.14	3.17 (7.7)	4.60	3.25 (HO-1') ($J_{1',OH}$ = 5.2)
7a	8.89	5.04 (3.4)	4.33 (6.4)	1.08	3.24, 3.19	8.88	7.42 (8.8)	8.14	3.17 (7.7)	4.60	2.80 (HO-2') ($J_{2',OH}$ = 6.0)
8a	8.94	5.08 (3.2)	4.31 (6.6)	1.15	3.23, 3.18	8.86	7.42 (8.8)	8.14	3.16 (7.6)	4.61, 4.59 (12.2)	
6b	8.92	5.02 (4.6)	4.30 (6.4)	1.22	3.23, 3.18	8.85	7.40 (8.8)	8.13	3.14 (7.6)	4.58, 4.56 (12.2)	3.57 (HO-1') ($J_{1',OH}$ = 5.3)
8b	9.09	5.20 (3.4)	4.41 (6.4)	1.20	3.22, 3.17	8.85	7.40 (8.8)	8.13	3.14 (7.6)	4.57, 4.55 (12.2)	
11	8.96	5.90 (4.9)	4.43 (6.6)	1.26			10.93 [H-N(3)]				2.16 (AcO-1') 2.45 (AcN-2)[a]
12	9.02	5.15 (4.2)	5.35 (6.6)	1.22			10.82 [H-N(3)]				2.14 (AcO-2') 2.45 (AcN-2)[a]

	Ribofuranosyl moiety						
	H-1 ($J_{1,2}$)	H-2 ($J_{2,3}$)	H-3 ($J_{3,4}$)	H-4 ($J_{4,5a}$)	H^a-5 ($J_{5a,5b}$)	H^b-5 ($J_{4,5b}$)	Other signals
6a	5.18 (1.4)	5.12 (4.9)	5.23 (6.3)	4.28 b	4.30 (11.5)	4.13 (5.4)	2.09, 2.08, 2.05 (AcO-2,3,5)
7a	5.07 (1.5)	5.33 (4.9)	5.39 (6.3)	4.36 b	4.33b b	4.30b b	2.16, 2.07, 2.06 (AcO-2,3,5)
8a[c]	5.38 (1.0)	5.12 (4.9)	5.19 (6.6)	4.26 (3.9)	4.24 (11.5)	4.06 (5.9)	2.12, 2.035, 2.025 (AcO-2,3,5)[d]
	4.90 (1.5)	5.29 (4.9)	5.33 (6.0)	4.28 b	4.30b b	4.26b b	2.14, 2.04, 2.03 (AcO-2,3,5)[d]
6b	5.47 (1.2)	5.57 (4.9)	5.78 (6.1)	4.70 (4.4)	4.69 (12.0)	4.52 (6.8)	8.05, 7.94, 7.89 [Bz(o)][e] 7.55-7.50 [Bz(*p*)], 7.40-7.32 [Bz(*m*)]
8b[c]	5.61 (0.9)	5.46 (5.1)	5.70 (6.8)	4.695 (4.6)	4.61 (11.7)	4.48 (6.1)	7.99, 7.91, 7.82 [Bz(o)][e,f] 7.53-7.46 [Bz(*p*)], 7.37-7.28 [Bz(*m*)]
	5.22 (1.2)	5.81 (5.1)	5.86 (6.5)	4.70 (4.4)	4.76 (11.5)	4.64 (6.3)	8.04, 7.96, 7.88 [Bz(o)][e,f] 7.53-7.46 [Bz(*p*)], 7.37-7.28 [Bz(*m*)]
11	5.16 (0.8)	4.93 (4.9)	5.11 (7.1)	4.26 (3.9)	4.22 (11.7)	4.05 (6.1)	2.05, 2.05, 2.02 (AcO-2,3,5)
12	4.90 (1.0)	5.31 (4.9)	5.33 (6.6)	4.34 (3.7)	4.32 (11.5)	4.29 (6.1)	2.06, 2.02, 2.01 (AcO-2,3,5)

[a] δ12.3-12.8 (br s, NH-2). [b] Uncertain because of overlapping with other signals. [c] Upper two lines for 2'-*O*-ribofuranosyl moiety, lower two lines for 1'-*O*-ribofuranosyl moiety. Correlations of protons were confirmed by 2D-COSY measurement. [d] The assignments of acetyl groups may have to be interchanged. [e] $J_{o,m}$ = 8.3-8.6, $J_{o,p}$ = 1.2-1.5 Hz. [f] The assignments of Bz(*o*) signals may have to be interchanged.

N^2-(N,N-Dimethylaminomethylene)-3-[2-(4-nitrophenyl)ethyl]-2'-O-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)biopterin (**6b**) *and N^2-(N,N-dimethylaminomethylene)-3-[2-(4-nitrophenyl)ethyl]-1',2'-bis-O-(2,3,5-*

tri-O-benzoyl-β-D-ribofuranosyl)biopterin (**8b**)

Analogous to the preceding procedure compound **4** (170 mg, 0.290 mmol) was treated with **5b** (295 mg, 0.585 mmol) and $SnCl_4$ (0.14 mL, 1.21 mmol) at rt for 20 h. The products were separated by column chromatography with 1:2 AcOEt-hexane and then 2% MeOH-$CHCl_3$ into two fractions.

The faster-eluting fraction [R_f 0.82 (*A*)] gave **8b** (69.5 mg, 18%) as a pale yellow powder: mp 98-99°C (from AcOEt-hexane); ^{1}H NMR, see Table 2. Anal. calc. for $C_{72}H_{63}N_7O_{19}$ (1330.31): C65.01, H4.77; found: C65.18, H4.61.

The slower-eluting fraction [R_f 0.60 (*A*)] gave **6b** (155 mg, 60%) as a pale yellow powder: mp 113-114°C (from AcOEt-hexane); ^{1}H NMR, see Table 2. Anal. calc. for $C_{46}H_{43}N_7O_{12}$ (885.87): C62.37, H4.89; found: C62.50, H4.98.

2'-O-(β-D-ribofuranosyl)biopterin (**1c**)

A. *Via* **9**. Compound **6b** (100 mg, 0.113 mmol) was dissolved in dry MeOH (5.0 mL) and 28% methanolic NaOMe (0.05 mL, 0.24 mmol) was added at 0°C. The mixture was stirred at rt for 2 h and neutralized with Amberlite IR120(H^+). The resin was filtered off and the filtrate was evaporated in vacuo. The residue was washed with ether to give N^2-(*N*,*N*-dimethylaminomethylene)-3-[2-(4-nitrophenyl)ethyl]-2'-*O*-(β-D-ribofuranosyl)biopterin (**9**) (63 mg) as a yellow amorphous solid: R_f 0.07 (A), 0.54 (*B*).

Compound **9** was dissolved in MeOH (8.0 mL) and 28% aqueous ammonia solution (8.0 mL) was added. The mixture was stirred at rt for 12 h and evaporated in vacuo. The residue was dissolved in DMF (2.0 mL) and then DBU (0.10 mL, 1.28 mmol) was added. The mixture was stirred at rt for 12 h, diluted with water (4.0 mL), and neutralized with Amberlite IRC50(H^+). The resin was filtered off and the filtrate was evaporated in vacuo. The residue was washed with $CHCl_3$ and dried under reduced pressure to give **1c** (36.4 mg, 87% from **6b**) as a yellow powder: R_f 0.36 (*B*); ^{1}H NMR [DMSO-d_6 (D_2O exchange)] δ 1.01 (3H, d, $J_{2',3'}$ 6.6 Hz, H_3-3'), 3.30 (1H, dd, $J_{5a,5b}$ 11.5, $J_{4,5b}$ 5.9 Hz, H_b-5*), 3.47 (1H, dd, $J_{4,5a}$ 3.2 Hz, H_a-5*), 3.56 (1H, dd, $J_{2,3}$ 4.5, $J_{1,2}$ 0.8 Hz, H-2*), 3.70 (1H, ddd, $J_{3,4}$ 6.8 Hz, H-4*), 3.715 (1H, dd, H-3*), 4.00 (1H, qd, $J_{1',2'}$ 4.4 Hz, H-2'), 4.60 (1H, d, H-1*), 4.84 (1H, d, H-1'), 8.71 (1H, s, H-7), *for glycosyl moiety.

B. *Via* **10**. Compound **6b** (89.0 mg, 0.100 mmol) was dissolved in DMF (2.0 mL) and DBU (0.10 mL, 1.28 mmol) was added. The mixture was stirred at rt for 24 h, diluted with MeOH (4.0 mL), and neutralized with Amberlite IRC50(H^+). The resin was filtered off and the filtrate was evaporated in vacuo. The residue was separated by column chromatography with 2% MeOH-$CHCl_3$ to give N^2-(*N*,*N*-dimethylaminomethylene)-2'-*O*-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)biopterin (**10**) [33.2 mg, 46% yield, R_f 0.49 (*A*)] and **6b** (27.6 mg, 31% recovery).

By employing the same procedures described above, compound **10** was treated with NaOMe in MeOH and then aqueous ammonia to give **1c** (14.3 mg, 84% from **10**).

C. From **11**. Compound **11** (26.0 mg, 0.0449 mmol) was dissolved in MeOH (2.0 mL) and 28% aqueous ammonia solution (1.0 mL) was added. The mixture was stirred at rt for 12 h and evaporated in vacuo to give **1c** (16.4 mg, 99%).

Di-N^2:1'-O-acetyl-2'-O-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)biopterin (**11**)

Compound **1c** (23.0 mg, 0.0623 mmol) was dissolved in pyridine (1.5 mL) and then acetic anhydride (0.5 mL) was added at 0°C. The mixture was stirred at rt for 12 h and evaporated in vacuo. The residue was purified by column chromatography with 2% MeOH-$CHCl_3$ as an eluant to give **11** (33.8 mg, 94%) as a pale yellow syrup: R_f 0.54 (*A*); ^{1}H NMR, see Table 2. Anal. calc. for $C_{24}H_{29}N_5O_{12}$ (579.51): C49.74, H5.04; found: C49.89, H5.20.

Di-N^2:2'-O-acetyl-1'-O-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)biopterin (**12**)

By use of same procedures for **1c** from **6b**, a mixture of **6a** and **7a** was converted into a mixture consisting of **1c** and 1'-*O*-(β-D-ribofuranosyl)biopterin (**1d**), which was then acetylated with acetic anhydride in pyridine to give an inseparable mixture of **11** and **12**.

^{1}H NMR for **1d** [DMSO-d_6 (D_2O exchange)] δ 1.02 (3H, d, $J_{2',3'}$ 6.4 Hz, H_3-3'), 3.45 (1H, dd, $J_{5a,5b}$ 11.7, $J_{4,5b}$ 4.4 Hz, H_b-5*), 3.60 (1H, dd, $J_{4,5a}$ 3.2 Hz, Ha-5*), 3.77 (1H, dd, $J_{3,4}$ 6.6, $J_{2,3}$ 4.6 Hz, H-3*), 3.78 (1H, ddd, H-4*), 3.95 (1H, qd, $J_{1',2'}$ 5.6 Hz, H-2'), 4.02 (1H, dd, $J_{1,2}$ 0.8 Hz, H-2*), 4.52 (1H, d, H-1*), 4.58 (1H, d, H-1'), 8.64 (1H, s, H-7), *for glycosyl moiety. ^{1}H NMR for **12**, see Table 2.

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