80. Synthesis of Biopterin from Neopterin? The Formation of Pyrrolo[1,2-*f*]pteridins upon Side-Chain Activation of Neopterin

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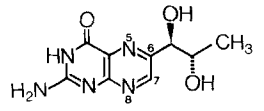
The formation of derivatives of L-neopterin (**2**) is investigated with respect to a possible transformation into L-biopterin (**1**). High-yield syntheses of isopropylidene and benzylidene derivatives **5** and **7**, respectively, are described. Activation of the primary C-atom in the side chain of neopterin leads to formation of pyrrolo[1,2-*f*]-pteridins *via* oxonium-ion intermediates.

Introduction. – (6*R*)-5,6,7,8-Tetrahydro-L-biopterin has been recognized to be the cofactor for phenylalanine, tyrosine, and tryptophan hydroxylases [1] and thus influences the biosynthesis of neurotransmitting catecholamines. Decrease of this tetrahydrobiopterin causes neurological disorders like atypical phenylketonuria [2] and *Parkinson*'s disease [3], but it may also be clinically relevant in the treatment of these diseases [4] [5]. Its precursor L-biopterin (**1**) is synthetically available, *e.g.* from 2,5,6-triamino-4-hydroxypyrimidine and 5-deoxy-L-arabinose [6] [7]; the latter has to be prepared in several steps from L-rhamnose [8] or D-glucose [9]. While the biopterin synthesis furnishes only fair yields, the analogous preparation of L-neopterin (**2**) (starting with 2,5,6-triamino-4-hydroxypyrimidine and commercially available L-arabinose) proceeds in a much cleaner way and gives high yields [10] [11]. Thus, reduction of the terminal OH group in the side chain of L-neopterin (**2**) would constitute an interesting synthesis of L-biopterin (**1**). Some results on the selective modification of L-neopterin are discussed in the following.

Results. – Since acylation (tosylation, acetylation, pivaloylation) of the primary OH function of L-neopterin (**2**) or transesterification [12] of the peracetate **3** [13] were not selective enough, we turned our attention to the formation of cyclic acetals of **2**. Reaction of L-neopterin with acetone/conc. H_2SO_4 50:1 or 2,2-dimethoxypropane/*p*-toluenesulfonic acid (TsOH) afforded 2',3'-*O*-isopropylideneneopterin (**4**) in 86 or 93% yield, respectively. This excellent regioselectivity is expected for an erythrose system [14]. The synthesis of the N^2,N^2-dimethyl analogue of **4** has been communicated recently in a review on the side-chain chemistry of pteridines [15].

O-Isopropylidene derivatives in terminal positions of carbohydrates are known to be converted to primary bromides by action of HBr/AcOH [16] [17]. Treatment of **4** with HBr/AcOH did not proceed satisfactorily, presumably due to the poor solubility of this compound. This problem was overcome by the use of diacetate **5**, readily obtained by standard acetylation of crude **4**. Bromination with HBr/AcOH led to *N*-(7-bromo-1,2-dihydro-1-oxopyrrolo[1,2-*f*]pteridin-3-yl)acetamide (**6**) as the major reaction product (judged by TLC), isolated in 22% yield.



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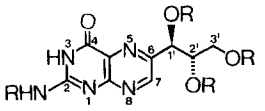
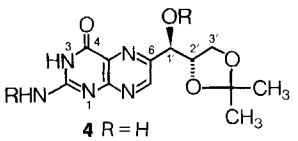


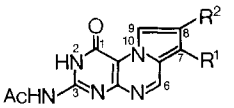
2 R = H

3 R = Ac



4 R = H

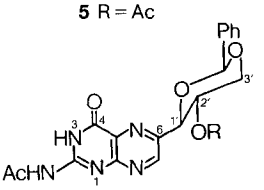
5 R = Ac



6 R^1 = Br, R^2 = H

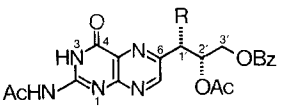
10 R^1 = OBz, R^2 = OAc

12 R^1 = OAc, R^2 = H



7 R = Ac

8 R = CH(OCH$_3$)Ph



9 R = Br

11 R = H

Ac = $-\overset{\overset{O}{\|}}{C}-CH_3$

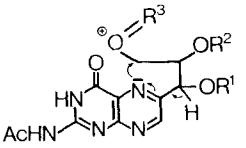
Bz = $-\overset{\overset{O}{\|}}{C}-Ph$, Ph = 

Next, the formation of an *O*-benzylidene derivative of L-neopterin (**2**) was investigated. Standard reaction conditions (α,α-dimethoxytoluene, TsOH, DMF [18]) gave an unseparable mixture of numerous benzylidene derivatives (^{1}H-NMR). Omission of solvent increased the regioselectivity of the reaction drastically to yield a dioxane-type acetal in a heterogeneous reaction. This product was best isolated after acetylation and chromatography as the diacetyl derivative **7** in excellent yield (90%). The presence of a six-membered-ring benzylidene acetal is evidenced by the coupling of the diaxial H–C(1′) and H–C(2′) (J(1′,2′) = 9.6 Hz) and the characteristic downfield shift of H–C(2′) after acetylation. Compound **8** was isolated as a minor by-product (the formation of mixed acetals is known in acetal-exchange reactions [19]). *N*-Bromosuccinimide (NBS) opening [20] of the benzylidene derivative **7** in CCl_4 in the presence of a radical initiator (benzoyl peroxide) furnished the 1′-bromo compound **9** as main product (80%) along with small amounts (6%) of pyrrolo[1,2-*f*]pteridin **10**. Brominating-benzylidene-ring opening at secondary C-atoms (here C(1′) of **7**) is known [21] to occur with inversion of configuration, and the configuration of the L-monapterin derivative **9** is deduced from its positive optical rotation (*cf.* [7] for an analogous 1′-chloro compound). The 1′-position of the Br-atom in **9** was corroborated by hydrogenation to the 1′-deoxy derivative **11**. The selectivity of this reaction was best using Pd/C in dioxane, whereas employment of Pt_2O furnished complex reaction mixtures.

Another pyrrolo-pteridin, namely **12**, was obtained as by-product in the acetylation of L-neopterin (**2**) with AcOH/conc. H_2SO_4 or with Ac_2O/AcOH according to [13]. The non-acetylated form of **12** has already been isolated after treatment of neopterin with polyphosphoric acid [22].

All three pyrrolo-pteridins **6**, **10**, and **12** exhibit similar UV spectra. Characteristically, H–C(9) appears as a broad signal in the ^{1}H-NMR spectra due to the proximity of the amide C=O group. Consistently, the IR absorption of this C=O is at lower energy compared to the neopterin derivatives. For the vicinal ^{1}H-NMR coupling constants in the pyrrole ring, J(8,9) = 2.8–2.9 Hz is found, as opposed to an allylic coupling constant of J(7,9) = 1.5 Hz in similar systems [23], thus supporting the structures assigned.

Discussion. – It is seen from the isolation of bromides **6** and **9** as main products that C(1′) is the preferred site of attack in the brominations of isopropylidene-neopterin **5** and benzylidene-neopterin **7**, respectively. Only of minor importance seems to be an attack at the primary C-atom C(3′). Both, the reaction of isopropylidene compounds in HBr/AcOH and the NBS opening of benzylidene acetals are postulated to proceed *via* intermediate oxonium ions [16] [24]. This activation of the terminal C-atom C(3′) of the neopterin side chain obviously occurs, however, it initiates the pyrrole-ring formation as depicted in **A**.



A

The formation of oxonium ions is also likely in the acid-catalyzed acetylation of neopterin (**2**→**3** + **12**), and this initiation of ring formation would be in keeping with the previously described [22] preparation of a pyrrolo-pteridin in the presence of polyphosphoric acid. The aromatic pyrrole ring would then result from elimination of a substituent at C(8) or C(9). Preservation of AcO–C(8) in **10** may be rationalized by another bromination at C(9) and subsequent elimination.

These results and considerations demonstrate that no high-yield synthesis of biopterin from neopterin can be expected due to pyrrolo-pteridin formation upon activation of the side-chain terminus of neopterin.

The skillful technical assistance of Mr. *R. Keller* is gratefully acknowledged. We also wish to thank our colleagues from the Central Research Department for determination of physical and analytical data: Dr. *W. Arnold* (NMR), Dr. *L. Chopard* (IR, UV), Dr. *A. Dirscherl* (MA), Dr. *M. Grosjean* (IR, UV), Mr. *W. Meister* (MS), and Dr. *W. Vetter* (MS).

Experimental Part

General. Solvents and reagents were obtained from *Fluka* (*puriss. p.a.*). Evaporation: *Büchi*-rotary evaporator, at 30–40°/*in vacuo*. TLC: precoated silica gel *60F-254* plates (*Merck*), detection by UV light (254 and 350 nm) and spraying with a 10% soln. of conc. H_2SO_4 in MeOH followed by heating. MPLC (medium pressure liquid chromatography): *Lobar* columns, *LiChroprep Si 60* (40–63 μm, Merck) at 2–5 bar (*Labomatic MD 80/100* pump). M.p. (uncorrected): *Büchi-510* apparatus. $[\alpha]_D$: *Perkin Elmer 241* polarimeter, 1 dm cell. UV: *Uvikon 810*. IR (cm^{-1}): *Nicolet-7199-FT-IR* spectrophotometer. ^{1}H-NMR: *Bruker AS-250* (250 MHz), *Bruker HX-270* (270 MHz), or *Bruker WM 400* (400 MHz), chemical shifts in ppm relative to tetramethylsilane as internal standard, coupling constants *J* in Hz.

*2′,3′-O-Isopropylidene-*L*-neopterin* (= *2-Amino-6-(1′-hydroxy-2′,3′-isopropylidenedioxypropyl)pteridin-4-(3*H*)-one;* **4**). To a stirred suspension of **2** (1.0 g, 3.95 mmol) [10] [11] in 2,2-dimethoxypropane (200 ml) was added TsOH (750 mg, 3.95 mmol). After stirring for 24 h at r.t., the mixture was evaporated to ½ the volume. Pyridine (2 ml) was added, and the solvents were evaporated. The residue was suspended in hot H_2O (50 ml), cooled, and filtered. The filter cake was suspended in MeOH (50 ml) and filtered when still warm to give **4** (1.174 g, 93%) as colourless crystals, m.p. > 250°. ^{1}H-NMR (270 MHz, (D_6)DMSO): 11.59 (br., NH(3)); 8.72 (*s*, H–C(7)): 6.98 (br., NH_2–C(2)); 5.89 (*d*, J = 4.5, OH–C(1′)); 4.60 (*dd*, $J(1',2')$ = 5.5, H–C(1′)); 4.41 (*ddd* ≈ *dt*, H–C(2′)); 4.04 (*dd*, $J(2',3a')$ = 6.3, $J(3a',3b')$ = 8.3, H_a–C(3′)); 3.93 (*dd*, $J(2',3b')$ = 5.7, H_b–C(3′)); 1.24 (*s*, CH_3); 1.21 (*s*, CH_3). EI-MS: 278 (8, $M^{+\cdot}-CH_3$), 193 (100, $M^{+\cdot}-C_5H_8O_2$), 101 (38, $C_5H_9O_2^+$). Anal. calc. for $C_{12}H_{15}N_5O_4 \cdot 0.6\ H_2O$ (304.09): C 47.40, H 5.36, N 23.06; found: C 47.54, H 5.32, N 22.78.

*2-N,1′-O-Diacetyl-2′,3′-O-isopropylidene-*L*-neopterin* (= *1′-(2-Acetamido-3,4-dihydro-4-oxopteridin-6-yl)-2′,3′-(isopropylidenedioxy)propyl Acetate;* **5**). After evaporation of the solvents, the residue **4** (see above; from 1 g

of **2**) was suspended in pyridine (100 ml) and Ac_2O (50 ml). The clear soln. obtained after stirring for 22 h was poured into ice/H_2O, extracted with CH_2Cl_2, the extract dried (Na_2SO_4), and evaporated. MPLC (acetone/hexane 2:1) gave 1.46 g (98%) of crystalline **5**, m.p. 201–204°. ^{1}H-NMR (250 MHz, (D$_6$)DMSO): 12.31 (br., NH(3)); 11.9 (br., NH–C(2)); 8.96 (*s*, H–C(7)); 5.77 (*d*, J(1',2') = 6.1, H–C(1')); 4.60 (*ddd* ≈ *dt*, H–C(2')); 4.12 (*dd*, J(2',3'a) = 6.5, J(3'a,3'b) = 8.9, H$_a$–C(3')); 4.01 (*dd*, J(2',3'b) = 5.0, H$_b$–C(3')); 2.22 (*s*, NAc); 2.10 (*s*, OAc); 1.23 (*s*, 2CH$_3$). EI-MS: 362 (10, $M^{+\cdot}$ – CH$_3$), 277 (22, $M^{+\cdot}$–C$_5$H$_8$O$_2$), 235 (62, $M^{+\cdot}$ – C$_5$H$_8$O$_2$ – C$_2$H$_2$O), 101 (23, C$_5$H$_9$O$_2^+$), 43 (100, C$_2$H$_3$O). Anal. calc. for C$_{16}$H$_{19}$N$_5$O$_6$ (377.357): C 50.93, H 5.08; found: C 50.95, H 5.18.

N-*(7-Bromo-1,2-dihydro-1-oxopyrrolo[1,2-f]pteridin-3-yl)acetamide* (**6**). To a freshly prepared sat. soln. of dry HBr in glacial AcOH (2 ml), **5** (400 mg, 1.06 mmol) was added stirring rigorously. After 20 min at 0°, the soln. was diluted with CH_2Cl_2 (20 ml) and poured onto ice/$NaHCO_3$ soln. The org. soln. was washed twice with H_2O, dried (Na_2SO_4), and evaporated. Treatment of the residue (327 mg) with hot acetone (10 ml) gave crude crystals (140 mg) that were recrystallized from MeON to yield dark-yellow crystals of pure **6** (75 mg, 22%), m.p. > 270°. UV (EtOH): 392 (3070), 348 (5330), 333 (5820), 295 (29 560), 283 (31 130), 244 (11 300), 202 (17 120). ^{1}H-NMR (270 MHz, (D$_6$)DMSO): 12.4 (br., NH(2)); 11.97 (*s*, NH–C(3)); 8.98 (*s*, H–C(6)); 8.88 (*d*, J = 2.8, H–C(9)); 7.18 (*d*, H–C(8)); 2.21 (*s*, NAc). EI-MS: 323/321 (45/50, $M^{+\cdot}$), 281/279 (96/100, $M^{+\cdot}$ – C$_2$H$_2$O), 200 (22, $M^{+\cdot}$ – C$_2$H$_2$O–Br), 43 (86, C$_2$H$_3$O).

*2-*N*,2'-*O*-Diacetyl-1',3'-*O*-benzylidene-*L*-neopterin* (= *[4-(2-Acetamido-3,4-dihydro-4-oxopteridin-6-yl)-2-phenyl-1,3-dioxan-5-yl] Acetate*; **7**) *and 2-*N*-Acetyl-1',3'-*O*-benzylidene-2'-*O*-(α-methoxybenzyl)-*L*-neopterin* (= *N-{3,4-Dihydro-6-[5-(α-methoxybenzyloxy)-2-phenyl-1,3-dioxan-4-yl]-4-oxopteridin-2-yl}acetamide*; **8**). To a suspension of **2** (1.0 g, 3.95 mmol) [10] [11] in α,α- dimethoxytoluene (35 ml) was added TsOH (750 mg, 3.95 mmol). After stirring for 48 h at r.t., Et_3N (10 ml) was added to the slurry, which was then evaporated at 60°. The residue was stirred with pyridine (50 ml) and Ac_2O (25 ml) for 4.5 h at r.t. The resulting soln. was poured into ice/$NaHCO_3$ soln. and extracted with CH_2Cl_2. Drying (Na_2SO_4), evaporation, and MPLC (acetone/hexane 1:1, 0.1% Et_3N) gave **8** (150 mg, 7.5%) followed by **7** (1.512 g, 90%). **7**: M.p. 250–251° (dec.; after precipitation from acetone), $[\alpha]_D^{20}$ = – 26.7° (*c* = 0.09, dioxane). ^{1}H-NMR (400 MHz, CDCl$_3$/(D$_6$)DMSO 3:1): 12.52 (*s*, NH(3)); 12.03 (*s*, NH–C(2)); 9.07 (*s*, H–C(7)); 7.56–7.53 (*m*, 2 arom. H); 7.40–7.38 (*m*, 3 arom. H); 5.78 (*s*, PhC*H*); 5.22 (*ddd* ≈ *dt*, H–C(2')); 5.15 (*d*, J(1',2') = 9.6, H–C(1')); 4.45 (*dd*, J(2',3a') = 5.2, J(3a,3b) = 10.0, H$_a$–C(3')); 3.96 (*dd* ≈ *t*, J(2',3b') = 10.0, H$_b$–C(3')); 2.28 (*s*, NAc); 1.99 (*s*, OAc). EI-MS: 365 (1, $M^{+\cdot}$ – C$_2$H$_4$O$_2$), 259 (54, 365 – C$_7$H$_6$O), 217 (30, 259 – C$_2$H$_2$O), 234 (50, $M^{+\cdot}$ – C$_{11}$H$_{11}$O$_3$), 192 (34, 234 – C$_2$H$_2$O), 107 (24, C$_7$H$_7$O), 105 (22, C$_7$H$_5$O), 43 (100, C$_2$H$_3$O). Anal. calc. for C$_{20}$H$_{19}$N$_5$O$_6$ (425.40): C 56.47, H 4.50, N 16.46; found: C 57.12, H 4.64, N 16.66.

8: ^{1}H-NMR (400 MHz, CDCl$_3$/(D$_6$)DMSO 3:1): 12.50 (br., NH(3)); 11.97 (br., NH–C(2)); 8.95 (*s*, H–C(7)); 7.57–7.30 (*m*, 10 arom. H); 5.72 (*s*, PhC*H*); 5.39 (*s*, PhC(OCH$_3$)*H*); 5.09 (*d*, J(1',2') = 9.2, H–C(1')); 4.49 (*dd*, J(2',3a') = 5.2, J(3a',3b') = 10.8, H$_a$–C(3')); 4.38 (*ddd*, H–C(2')); 3.93 (*dd* ≈ *t*, J(2',3b') = 10.0, H$_b$–C(3')); 3.14 (*s*, CH$_3$O); 2.29 (*s*, NAc).

*2-*N*-Acetyl-6-[(1'*S*,2'*S*)-2'-acetoxy-3'-(benzoyloxy)-1'-bromopropyl]pterin* (= *[3-(2-Acetamido-3,4-dihydro-4-oxopteridin-6-yl)-2-acetoxy-3-bromopropyl] Benzoate*; **9**) *and [3-Acetamido-8-acetoxy-1,2-dihydro-1-oxopyrrolo[1,2-f]pteridin-7-yl] Benzoate* (**10**). To a warm soln. of **7** (500 mg, 1.175 mmol) in CCl_4 (200 ml; dried over activated (300°) molecular sieves, 4 Å) containing small amounts of $BaCO_3$ and benzoyl peroxide was added NBS (314 mg, 1.77 mmol). After refluxing for 4.5 h under Ar, the mixture was cooled, poured onto ice/H_2O and extracted with CH_2Cl_2. Drying (Na_2SO_4) and evaporation followed by MPLC (acetone/hexane 1:1; sample applied in CH_2Cl_2 soln.) yielded **9** (477 mg, 80%) followed by **10** (30 mg, 6%). **9**: Colourless amorphous solid, $[\alpha]_D^{20}$ = + 28.7° (*c* = 0.3, dioxane). UV (EtOH): 337 (8750), 289 (15 860), 229 (23 500), 201 (26 930). ^{1}H-NMR (270 MHz, CDCl$_3$): 12.85 (br., NH(3)); 11.10 (br., NH–C(2)); 9.14 (*s*, H–C(7)); 7.96 (*m*, 2 arom. H); 7.58 (*m*, 1 arom. H); 7.44 (*m*, 2 arom. H); 5.87 (*ddd* ≈ *q*, H–C(2')); 5.55 (*d*, J(1',2') = 6.0, H–C(1')); 4.59 (*dd*, J(2,3a') = 4.7, J(3a',3b') = 12.0, H$_a$–C(3)); 4.48 (*dd*, J(2',3b') = 5.7, H$_b$–C(3')); 2.18 (*s*, 2 CH$_3$). EI-MS: 424 (0.4, $M^{+\cdot}$ – Br), 364 (1, 424 – C$_2$H$_4$O$_2$), 322/324 (1/1, $M^{+\cdot}$ – C$_6$H$_5$ – COOH – C$_2$H$_3$O$_2$), 259 (36, 322/324 – Br$^\cdot$), 217 (50, 259 – C$_2$H$_2$O), 122 (44, C$_6$H$_5$COOH), 105 (100, 122 – OH), 77 (62, 105 – CO), 43 (73, C$_2$H$_3$O). Anal. calc. for C$_{20}$H$_{18}$BrN$_5$O$_6$ · 0.4 C$_6$H$_{14}$ (538.77): C 49.29, H 4.42, Br 14.83, N 13.00; found: C 49.50, H 4.45, Br 14.21, N 13.05.

10: Yellow crystals, m.p. > 260°. ^{1}H-NMR (270 MHz, (D$_6$)DMSO): 12.47 (br., NH(2)); 11.92 (br., NH–C(3)); 9.14 (br., H–C(9)); 9.08 (*s*, H–C(6)); 8.15 (*m*, 2 arom. H); 7.79 (*m*, 1 arom. H); 7.64 (*m*, 2 arom. H); 2.40 (*s*, OAc); 2.21 (*s*, NAc). EI-MS: 421 (1, $M^{+\cdot}$), 379 (16, $M^{+\cdot}$ – C$_2$H$_2$O), 105 (100, C$_6$H$_5$CO$^+$).

*2-*N*-Acetyl-6-[(2'*R*)-2'-acetoxy-3'-(benzoyloxy)propyl]pterin* (= *[3-(2-Acetamido-3,4-dihydro-4-oxopteridin-6-yl)-2-acetoxypropyl] Benzoate*; **11**). To a pre-hydrogenated suspension of 5% Pd/C (40 mg) in dioxane (2 ml) was added a soln. of **9** (100 mg, 0.198 mmol) in dioxane (3 ml). After hydrogenation for 5 h at r.t., the mixture was filtered over a pad of *Speedex*, evaporated, and chromatographed (MPLC, acetone/hexane 3:2). The main fraction was precipitated from acetone/Et_2O to yield **11** (20 mg, 24%) as amorphous solid. ^{1}H-NMR (270 MHz, CDCl$_3$): 12.85 (br., NH(3)); 11.08 (br., NH–C(2)); 8.86 (*s*, H–C(7)); 8.03 (*m*, 2 arom. H); 7.59 (*m*, 1 arom. H); 7.46 (*m*, 2

arom. H); 5.66 (*ddt*, H–C(2')); 4.69 (*dd*, $J(2',3a') = 5.2$, $J(3a',3b') = 12.0$, H_a–C(3')); 4.64 (*dd*, $J(2',3b') = 3.4$, H_b–C(3')); 3.44 (*d*, $J(1',2') = 6.3$, 2 H–C(1')); 2.52 (*s*, NAc); 2.03 (*s*, OAc). EI-MS: 365 (4, $M^{+\cdot} - C_2H_4O_2$), 260 (22, 365 – $C_6H_5CO^{\cdot}$), 244 (50, 365 – $C_6H_5COO^{\cdot}$), 218 (18, 260 – C_2H_2O), 202 (18, 244 – C_2H_2O), 122 (12, C_6H_5COOH), 105 (100, $C_6H_5CO^+$), 77 (38, $C_6H_5^+$), 60 (6, $C_2H_4O_2$), 43 (40, C_2H_3O).

*2-*N*-Acetyl-1',2',3'-tri-*O*-acetyl-*L*-neopterin (= 1-(2-Acetamido-3,4-dihydro-4-oxopteridin-6-yl)propan-1,2,3-triyl Triacetate; **3**) and [3-Acetamido-1,2-dihydro-1-oxopyrrolo[1,2-f]pteridin-7-yl] Acetate* (**12**). To a suspension of **2** (200 mg, 0.79 mmol) [10] [11] in Ac_2O (10 ml) was added conc. H_2SO_4 (0.4 ml) dropwise. After stirring for 16 h at r.t., a yellow soln. was obtained. Upon addition of Et_3N (1 ml), the mixture was poured into ice/H_2O and extracted with CH_2Cl_2. The combined org. soln. was dried ($MgSO_4$), evaporated, and coevaporated with toluene repeatedly. The resulting yellow foam was crystallized from MeOH to give **12** (27 mg, 11%). The mother liquor was evaporated *i.v.* and purified by MPLC (acetone/hexane 3:2) yielding **3** (254 mg, 85%). **3**: Foam, $[\alpha]_D^{20} = -77.5°$ ($c = 0.2$, $CHCl_3$) ([13]: $[\alpha]_D^{23} = -76.5°$ ($c = 2.7$, $CHCl_3$)). UV (EtOH): 331 (7770), 283 (16200), 201 (14960). IR (KBr): 3427*w*, 3189*m*, 3024*w*, 2985*w*, 1748*s*, 1694*s*, 1626*s*, 1565*s*, 1496*m*, 1456*s*, 1970*s*, 1224*s*, 1128*w*, 1048*m*, 954*w*, 827*w*, 784*w*, 733*w*, 603*w*. ^{1}H-NMR (270 MHz, (D_6)DMSO): 12.33 (br., NH(3)); 12.02 (br., NH–C(2)); 8.99 (*s*, H–C(7)); 6.03 (*d*, $J(1',2') = 5.7$, H–C(1')); 5.54 (*ddd*, H–C(2')); 4.31 (*dd*, $J(2',3'a) = 4.5$, $J(3'a,3'b) = 12.0$, H_a–C(3')); 4.27 (*dd*, $J(2',3b') = 6.4$, H_b–C(3')); 2.22 (*s*, NAc); 2.16 (*s*, OAc); 1.96 (*s*, OAc); 1.95 (*s*, OAc). EI-MS: 379 (3, $M^{+\cdot} - C_2H_2O$), 361 (2, $M^{+\cdot} - C_2H_4O_2$), 319 (20, 361 – C_2H_2O), 277 (12, 319 – C_2H_2O), 235 (45, 277 – C_2H_3O), 43 (100, $C_2H_3O^+$). Anal. calc. for $C_{17}H_{19}N_5O_8$ (421.37): C 48.46, H 4.55, N 16.62; found: C 48.31, H 4.79, N 16.34.

12: Yellow crystals, m.p. > 260°. UV (EtOH): 392 (2600), 348 (5080), 333 (5810), 294 (29310), 283 (30880), 243 (12080), 206 (12080), 206 (19610). IR (KBr): 3430 (br.), 3144*m*, 2925*m*, 2854 (sh), 2790 (sh), 1778 (sh), 1761*m*, 1672*s*, 1629*s*, 1587*s*, 1537*m*, 1482*m*, 1446*m*, 1369*s*, 1341*w*, 1304*s*, 1218*s*, 1190*s*, 1112*m*, 1048*m*, 1009*w*, 952*w*, 884*m*, 866 (sh), 785*m*, 758*w*, 720*w*. ^{1}H-NMR (270 MHz, (D_6)DMSO): 12.45 (br., NH(2)); 11.90 (br., NH–C(3)); 9.02 (*s*, H–C(6)); 8.80 (br., H–C(9)); 6.93 (*d*, $J(8,9) = 2.9$, H–C(8)); 2.38 (*s*, Ac); 2.20 (*s*, Ac). EI-MS: 301 (16, $M^{+\cdot}$), 259 (76, $M^{+\cdot} - C_2H_2O$), 217 (100, 259 – C_2H_2O), 43 (42, C_2H_3O). Anal. calc. for $C_{13}H_{11}N_5O_4 \cdot 0.5\,CH_3OH$ (317.28): C 51.11, H 4.13, N 22.07; found: C 51.48, H 3.84, N 21.81.

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