29. Stereoselective Synthesis of Indazole 2'-Deoxy-β-D-ribonucleosides: Glycosylation of the Nucleobase Anion

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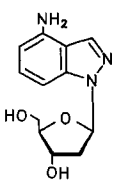
The glycosylation of indazolyl anions derived from **4a, b** with 2-deoxy-3,5-bis-*O*-(4-methylbenzoyl)-α-D-*erythro*-pentofuranosyl chloride (**5**) is described. The reaction was stereoselective – exclusive β-D-anomer formation – but regioisomeric N^1- and N^2-(2'-deoxy-β-D-ribofuranosides) (*i.e.* **6a** and **7a**, resp., and **6b** and **7b**, resp.) were formed in about equal amounts. They were deprotected to yield **8a, b** and **9a, b**. Compound **1**, related to 2'-deoxyadenosine (**3**), and its regioisomer **2** were obtained from **8b** and **9b**, respectively, by catalytic hydrogenation. The anomeric configuration as well as the position of glycosylation were determined by 1D NOE-difference spectroscopy. The first protonation site of **1** and **2** was found to be the NH_2 group. The *N*-glycosylic bond of 1*H*-indazole N^1-(2'-deoxyribofuranosides) is more stable than that of the parent purine nucleosides. Compound **1** is no substrate for adenosine deaminase.

Introduction. – The 1*H*-indazole (**4a**) [1] is structurally related to 1*H*-benzimidazole [2]. Regarding the pyrazole moiety of **4a**, similarities exist also between indazoles and pyrazolo[3,4-*d*]pyrimidines [3]. Several indazoles exhibit biological (*e.g.* antitrypanozoidal) [4] or antiallergic [5] activity or function as antagonists of serotonine receptors [6]. Indazole ribonucleosides [7–12] or xylonucleosides [13] as well as other glycosyl indazoles [14] [15] have already been synthesized. Indazole ribonucleotides have been prepared by enzymatic ribosylation employing NADase [16–18]. Surprisingly, indazole 2'-deoxyribonucleosides are unknown.

Earlier, we reported on the syntheses of benzimidazole [19] and pyrazolo[3,4-*d*]pyrimidine 2'-deoxyribonucleosides [20] [21] both related to indazole 2'-deoxyribonucleosides. In the following, the glycosylation of indazolyl anions is studied [22] with respect to the syntheses of the 2'-deoxyribonucleosides **1** and **2**, derivatives of 2'-deoxyadenosine (**3**). Furthermore, the hydrolytic stability of 4-amino-1*H*-indazole 2'-deoxyribonucleosides is investigated, and the site of protonation is determined.



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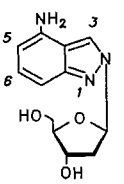

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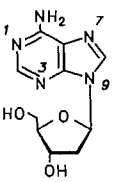

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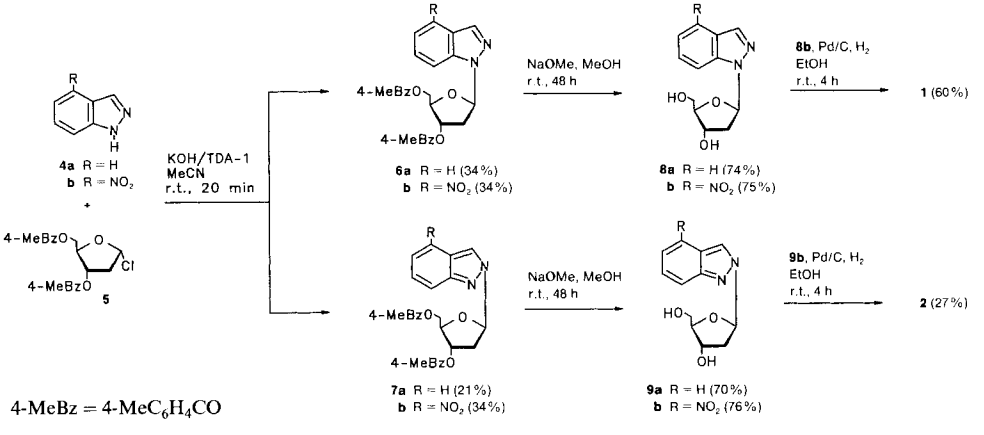
Results and Discussion. – Previous investigations on indazole D-ribonucleosides showed that silylated bases gave rise to the formation of N^2-glycosides preferentially [7] [8] [14] [15]; N^1-isomers were formed under conditions of the fusion reaction using *O*-acetyl-D-ribose derivatives [23] [24]. Although the fusion reaction is a facile procedure, it is not stereospecific, the elevated temperature and/or the acidic conditions leading to anomeric mixtures [24] [11]. Such condensation methods, as well as others leading exclusively to indazole N^1-ribonucleosides, cannot be employed for the synthesis of indazole 2′-deoxy-D-ribonucleosides. Indeed, the absence of a participating group at C(2) of 2-deoxy-α-D-ribofuranosyl halides causes the formation of anomeric mixtures on glycosylation. We have developed a stereoselective synthesis of 2′-deoxy-β-D-ribonucleosides employing nucleobase anions [25] [26] and have applied this method to the syntheses of several 2′-deoxyribonucleosides containing base moieties different from purine moieties [27–29]. Within these studies, it became apparent that heterocycles containing more than one nucleophilic centre gave rise to the formation of regioisomers. The ratio depended both on the particular heterocyclic system and on the pattern of substituents.

Initially, 1*H*-indazole (**4a**) was selected for glycosylation experiments. Compound **4a** has already been glycosylated with other ribose derivatives employing different glycosylation techniques [7] [10]. Its nitro derivative **4b** was chosen as it is a direct precursor for the syntheses of compounds **1** and **2**. Compound **4b** was prepared from 2-methyl-3-nitroaniline *via* its diazonium salt; intramolecular cyclization afforded the heterocycle [31]. Indazole **4a** is a weak acid (pK_{BH^+} 14.0, identical to that of pyrazole [32]), and as the nitro group increases acidity, the alkali salt of **4b** should also be readily formed. The generation of the *N*-anion of **4a** or **4b** was performed under solid-liquid phase-transfer conditions in MeCN containing a three fold excess of powdered KOH and of the cryptand tris[2-(2-methoxyethoxy)ethyl]amine (TDA-1) [33]. Glycosylation with 2-deoxyhalogenose **5** [34] proceeded then at room temperature stereoselectively within 20 min to give the regioisomeric mixtures **6a**/**7a** (1.6:1) and **6b**/**7b** (1:1), respectively (TLC), which were separated by flash chromatography (**6a**, **7b** faster migrating than **6b**, **7a**). The glycosylation of the indazolyl anion of **4a**, **b** thus gave similar ratios of N^1/N^2-regioisomers as the methylation

Scheme 1



of **4a, b** [32]. The corresponding ratio was 1.25:1 in the case of the benzimidazole N^1/N^3-nucleosides [19] and 2.0:1 in the case of the pyrazolo[3,4-*d*]pyrimidine N^1/N^2-nucleosides [20] [21]; however, the 4-substituent was different in these cases.

Compounds **6a, b** and **7a, b** were deprotected (NaOMe/MeOH) affording the indazole 2′-deoxynucleosides **8a, b** and **9a, b**, respectively. These were purified by flash chromatography. Finally, the nitro nucleosides **8b** and **9b** were hydrogenated under normal pressure (Pd/C) to give the amino nucleosides **1** and **2**, respectively. While compound **1** was isolated in 60% yield, the N^2-regioisomer was obtained in only 27% yield due to partial decomposition during chromatography.

Structural assignment of indazole nucleosides has hitherto been performed by comparison of their UV spectra with those of the *N*-alkylated derivatives [35–38]. In this publication, ^{1}H-NMR NOE difference spectroscopy is used for both the assignment of the anomeric configuration and the determination of the glycosylation site [39] (*Table 1*). Upon irradiation of H–C(1′), the N^1-regioisomers **8a** and **8b** show NOE's for H–C(7) and the N^2-compounds **9a** and **9b** for H–C(3); both regioisomers show NOE's for H_α–C(2′) and H–C(4′) proving β-D-configuration.

Table 1. *NOE Data of Indazole 2′-Deoxyribonucleosides in (D_6)DMSO at 23°*

Compound	Irradiated H	Observed NOE (%)
1	H–C(1′)	H–C(7) (10.7); H–C(4′) (1.6); H_α–C(2′) (7.1)
2	H–C(1′)	H–C(3) (7.1); H_α–C(2′) (7.3); H–C(4′) (1.3)
	NH_2	H–C(3) (9.7); H–C(5) (9.9)
8a	H–C(1′)	H–C(7) (11.1)[a]); H–C(4′) (1.4); H_α–C(2′) (6.5)
8b	H–C(1′)	H–C(7) (11.8); H–C(4′) (1.8); H_α–C(2′) (7.4)
9a	H–C(1′)	H–C(3) (7.9); H–C(4′) (1.4); H_α–C(2′) (5.9)
	H–C(3)	H–C(4) (3.5); H–C(1′) (6.6); H–C(3′) (0.7); H_β–C(2′) (1.1)
	H–C(4)	H–C(3) (2.6); H–C(5) (10.0)
9b	H–C(1′)	H–C(3) (10.2); H_α–C(2′) (7.5); H–C(4′) (1.5)

[a]) Superimposed by H–C(4).

Regarding the assignment of the ^{13}C-NMR chemical shifts of indazole nucleosides [40] [41] (*Table 2*), successive NOE measurements were carried out to identify the chemical shifts of the aromatic protons (*Table 1*) [42] [43]. ^{1}H,^{13}C-Correlation spectra then allowed the assignment of the signals of H-carrying C-atoms.

Differentiation between C(3a) and C(7a) is made on estimated downfield shifts induced by N(1). Compared to the parent **8a**, introduction of the NO_2 group (see **8b**) or the NH_2 group at C(4) (see **1**) results in a downfield shift of the C(4) signal by *ca.* 20 ppm; as expected, the atoms in *meta* position are not affected. The same situation is found for the N^2-regioisomers. Similarly to pyrazolo[3,4-*d*]pyrimidine nucleosides [20] [21], the N^2-isomers **2**, **7a, b**, and **9a, b** show a significant downfield shift of the *H*–C(3) *s* (0.29–0.55 ppm) compared to the N^1-isomers **1**, **6a, b**, and **8a, b**, respectively. On the other hand, *H*–C(1′) of the N^2-isomers is shifted upfield (0.13–0.19 ppm). The chemical-shift difference of the diastereoisotopic *H*–C(2′) is > 0.59 ppm for N^1-isomers and < 0.31 ppm for the N^2-isomers. The sequence of the δ(C)'s of the sugar moiety (from low to high field) is C(1′), C(4′), C(3′), C(5′), and C(2′) in the case of the toluoyl-protected species and the deprotected N^2-isomers, whereas the deprotected N^1-isomers follow the order C(4′), C(1′), C(3′), C(5′), and C(2′). From a comparison of the C(3) and C(1′) signals, the glycosylation position can be deduced from the ^{13}C-NMR spectra: the C(3) signals of the N^2-isomers appear at higher field (10 ppm) than those of the N^1-isomers; an opposite shift is observed for C(1′) (*ca.* 5 ppm).

Table 2. *^{13}C-NMR Chemical Shifts of Indazole 2′-Deoxyribonucleosides*[a])

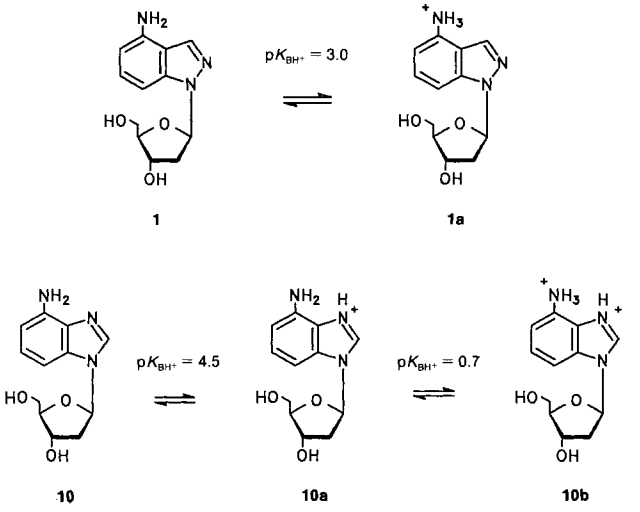
	C(3)	C(3a)	C(4)	C(5)	C(6)	C(7)	C(7a)
1	132.9	114.2	142.3[b])	102.3	128.2	96.4	141.4[b])
2	121.6	114.3	142.0	99.5	127.9	103.8	149.5
4b	132.2	115.2	141.9[b])	118.7	125.5	118.2	139.6[b])
6a	134.8	124.3	121.3	121.0	126.6	109.9	139.9
b	133.3	116.8	141.4[b])	119.1	126.5	118.1	139.7[b])
7a	124.1	121.1	121.0	121.5	129.3	117.5	148.4
b	124.9	113.6	140.3	121.0	125.4	126.6	149.4
8a	134.1	124.1	121.1	120.9	126.5	109.9	139.7
b	132.7	116.6	141.2[b])	118.9	126.3	118.1	139.6[b])
9a	122.9	121.0	120.9	121.3	126.0	117.3	148.0
b	123.8	113.6	140.3	120.8	125.1	126.6	149.1

	C(1′)	C(2′)	C(3′)	C(4′)	C(5′)	2 C=O	2 CH_3O
1	85.4	38.2	71.2	87.3	62.5		
2	90.3	DMSO	70.9	88.2	62.3		
6a	85.7	35.5	75.1	81.2	64.2	165.38, 165.43	21.1, 21.2
b	86.2	35.6	74.8	81.7	63.7	165.3, 165.4	21.1, 21.2
7a	90.2	37.0	75.0	82.2	64.2	165.3, 165.5	21.1, 21.2
b	90.6	37.2	74.7	82.6	63.8	165.3, 165.4	21.1, 21.2
8a	85.5	38.2	71.1	87.4	62.4		
b	86.2	38.3	70.9	87.8	62.2		
9a	90.5	40.7	70.6	88.3	62.0		
b	91.0	40.7	70.3	88.5	61.6		

[a]) In (D_6)DMSO. [b]) Tentative.

Indazole has a pK_{BH^+} of 1.22 which is lower than that of pyrazole (2.53) [32]. Due to its cyclic amidine structure, benzimidazole is much more basic (pK_{BH^+} 5.53). The pK values of **1** and **2** were determined in *Teorell-Stenhagen* buffer [44] and were found to be 3.0 for **1** and 3.6 for **2**. This led to the assumption that not the ring N-atom but the exocyclic NH_2 group is the site of protonation in the case of 4-aminoindazole nucleosides. In a previous publication [45], the UV spectra of 4-unsubstituted and 4-amino-substituted benzotriazole 2′-deoxyribofuranosides, both measured under neutral and acidic conditions, were compared and used to identify the NH_2 group as the protonation site. This method is now applied to **1** and **2**. Under neutral conditions, the UV spectra of the 4-amino nucleoside **1** (λ_{max} = 308 nm) is significantly different from that of the 4-unsubstituted **8a** (λ_{max} = 297 nm). However, in 0.5N HCl, they become very similar (**1**: 286 nm; **8a**: 285 nm). Corresponding results are found for the N^2-compounds **2** and **9a**. The resemblance of the UV spectra of the 4-amino compounds with that of the 4-unsubstituted derivatives measured under acidic conditions is the result of the uncoupling of the free NH_2 electron pairs from the aromatic system. Consequently, this group is the site of protonation, and the pK_{BH^+} of 3.0 refers to the process **1** ⇄ **1a** (*Scheme 2*); in analogy, the pK_{BH^+} of 3.6 is assigned to the NH_2 protonation of **2**. Protonation studies on the recently reported benzimidazole 2′-deoxy-β-D-ribofuranoside **10** [19] led to a different result. Here, the first protonation site is the imidazole N-atom (→ **10a**; pK_{BH^+} 4.5), whereas the second one is the NH_2 group (→ **10b**; pK_{BH^+} *ca.* 0.7; *Scheme 2*).

Scheme 2



Purine 2′-deoxyribonucleosides, in particular 2′-deoxyadenosine (**3**), are sensitive to acidic conditions suffering from hydrolysis of the *N*-glycosylic bond. As this is a severe drawback upon incorporation of purine nucleosides into oligonucleotides (proton-catalyzed detritylation), the hydrolytic stability of compounds **1** and **2** in HCl was studied by UV spectrophotometry and compared with the one of **3**. *Table 3* summarizes the corresponding half-life values and rate constants for the hydrolysis. The proton-catalyzed hydrolysis of purine nucleosides has been established to proceed by a rate-limiting formation of a cyclic glycofuranosyl oxocarbenium ion [46]. In contrast, 7-deazapurine nucleosides have been shown to be hydrolyzed *via* cationic *Schiff* bases with concurrent isomerization of the sugar moiety [47]. The results of the hydrolysis of the indazole ribonucleosides **1** and **2** gave strong evidence for a similar *N*-glycosylic-bond hydrolysis mechanism in the case of indazole and purine ribonucleosides. According to the p*K* values of indazoles [32] and indazole ribonucleosides [12], these compounds are extremely weakly basic at the ring N-atoms. This fact may explain the significantly higher stability of **1** compared to 2′-deoxyadenosine (**3**). Protonation at the exocyclic NH_2 group, as found for **1**, reduces the electron density of the nucleobase, but the charge delocalization is restricted compared to the protonation at a ring N-atom. Therefore, the ability of the nucleobase of **1** to act as leaving group is reduced.

Table 3. *Half-life Values* ($\tau/2$) *and First-Order Rate Constants* (k) *for Proton-Catalyzed Hydrolysis of 2′-Deoxyribonucleosides*[a])

Compound	$\tau/2$ [min] ($k \cdot 10^3$ [min^{-1}])	Hydrolysis conditions
1	92 (7.5)	1N HCl, 40°
2	20 (34.7)	0.1N HCl, 25°
3	3.5 (198)	1N HCl, 25°

[a]) Wavelength: **1**, 298 nm; **2**, 268 nm; **3**, 253 nm.

Regarding enzyme-catalyzed deamination, compound **1** is resistant to adenosine deaminase, like the corresponding benzimidazole 2′-deoxyribonucleoside. This has not necessarily to be attributed to enzymic recognition of the particular N-pattern of **1** but can be simply explained by the strongly decreased reactivity of the 4-NH_2 group upon nucleophilic displacement.

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Experimental Part

General. MeCN was distilled from CaH_2. Solvent systems: *A* = CH_2Cl_2/AcOEt 99:1, *B* = $CHCl_3$/MeOH 9:1, *C* = AcOEt/light petroleum 1:4, *D* = CH_2Cl_2/MeOH 95:5. TLC: glass plates coated with a 0.25-mm layer of silica gel *Sil G-25* with fluorescent indicator UV_{254} (*Merck*, FRG). Column flash chromatography (FC): 0.8 bar, silica gel *60 H* (*Merck*, FRG); connection to *Uvicord S* detector with a *MultiRac* fractions collector (*LKB Instruments*, Sweden). M.p.: *SMP-20* apparatus (*Büchi*, Switzerland). UV Spectra: *150–20* spectrophotometer (*Hitachi*, Japan). NMR spectra: *AC-250-Bruker* spectrometer, operational frequencies 250.134 (^{1}H) and 62.898 (^{13}C) MHz, values rel. to Me_4Si as internal standard. Microanalyses: *Mikroanalytisches Laboratorium Beller* (Göttingen, FRG).

Glycosylation of **4a** *with 2-Deoxy-3,5-bis-*O*-(4-methylbenzoyl)-α-*D-erythro-*pentofuranosyl Chloride* (**5**). Powdered KOH (1.18 g, 21.12 mmol) and tris[2-(2-methoxyethoxy)ethyl]amine (TDA-1; 175 mg, 0.59 mmol) were added to a soln. of 1*H*-indazole (**4a**; 1.0 g, 8.47 mmol) in anh. MeCN (75 ml). The mixture was stirred at r.t. for 10 min. Then **5** (3.44 g, 8.87 mmol) [34] was added within 5 min and stirring continued at r.t. for another 20 min. The mixture was filtered and the solvent evaporated. The resultant oil was chromatographed on a silica gel *60 H* (column: 40 × 5 cm, *A*).

*1-[2′-Deoxy-3′,5′-bis-*O*-(4-methylbenzoyl)-β-*D-erythro-*pentofuranosyl]-1*H*-indazole* (**6a**). From the zone with R_f 0.27, **6a** was obtained as a colorless oil which crystallized upon storage (1.35 g, 34%). UV (MeOH): 240 (35600), 278 (sh, 4700), 282 (5100), 298 (sh, 3600). ^{1}H-NMR ((D$_6$)DMSO): 2.39, 2.42 (2*s*, 2 CH_3); 2.76 (*ddd*, *J* = 4.1, 6.6, 13.6, $H_α$–C(2′)); 3.43 (‘*q*’, *J* = 6.7, $H_β$–C(2′)); 4.36 (*dd*, *J* = 5.3, 11.3, 1 H–C(5′)); 4.52 (*m*, H–C(4′), 1 H–C(5)); 5.88 (*m*, H–C(3′)); 6.90 (‘*t*’, *J* = 6.2, H–C(1′)); 7.19–8.01 (*m*, H–C(4), H–C(5), H–C(6), H–C(7), 8 arom. H); 8.25 (*s*, H–C(3)). Anal. calc. for $C_{28}H_{26}N_2O_5$: C 71.48, H 5.57, N 5.95; found: C 71.70, H 5.61, N 5.97.

*2-[2′-Deoxy-3′,5′-bis-*O*-(4-methylbenzoyl)-β-*D-erythro-*pentofuranosyl]-2*H*-indazole* (**7a**). The zone with R_f 0.20 afforded **7a** (836 mg, 21%) as a colorless oil which crystallized upon storage. UV (MeOH): 240 (33100), 275 (8700), 295 (sh, 6000), 306 (sh, 4000). ^{1}H-NMR ((D$_6$)DMSO): 2.36, 2.40 (2*s*, 2 CH_3); 2.82 (*m*, $H_α$–C(2′)); 3.27 (*m*, $H_β$–C(2′)); 4.46–4.66 (*m*, H–C(4′), 2 H–C(5′)); 5.88 (*m*, H–C(3′)); 6.68 (‘*t*’, *J* = 6.0, H–C(1′)); 7.03–7.97 (*m*, H–C(4), H–C(5), H–C(6), H–C(7), 8 arom. H); 8.60 (*s*, H–C(3)). Anal. calc. for $C_{28}H_{26}N_2O_5$: C 71.48, H 5.57, N 5.95; found: C 71.60, H 5.48, N 5.99.

*1-(2′-Deoxy-β-*D-erythro-*pentofuranosyl)-1*H*-indazole* (**8a**). Compound **6a** (1.0 g, 2.13 mmol) was dissolved in a mixture of MeOH (200 ml) and 1M NaOMe/MeOH (4.5 ml). The soln. was stirred at r.t. for 48 h. The solvent was evaporated at reduced pressure and the residue applied to FC (4 × 30 cm). Elution with *B* yielded a colorless oil (368 mg, 74%). TLC (*B*): R_f 0.47. UV (MeOH): 209 (27800), 251 (4900), 257 (sh, 4300), 288 (4500), 297 (sh, 3600). ^{1}H-NMR ((D$_6$)DMSO): 2.33 (*m*, $H_α$–C(2′)); 2.97 (*m*, $H_β$–C(2′)); 3.45 (*m*, 2 H–C(5′)); 3.88 (*m*, H–C(4′)); 4.51 (*m*, H–C(3′)); 4.76 (*t*, *J* = 5.5, OH–C(5′)); 5.32 (*d*, *J* = 4.4, OH–C(3′)); 6.63 (‘*t*’, *J* = 6.3, H–C(1′)), 7.20 (‘*t*’, *J* = 7.1, H–C(5) or H–C(6)); 7.43 (‘*t*’, *J* = 7.7, H–C(5) or H–C(6)); 7.79 (*m*, H–C(4), H–C(7)); 8.18 (*s*, H–C(3)). Anal. calc. for $C_{12}H_{14}N_2O_3$: C 61.53, H 6.02, N 11.96; found: C 61.54, H 6.06, N 11.84.

*2-(2′-Deoxy-β-*D-erythro-*pentofuranosyl)-2*H*-indazole* (**9a**). Compound **7a** (1.0 g, 2.13 mmol) was treated as described for **6a**. An oil was isolated which crystallized upon storage (348 mg, 70%). TLC (*B*): R_f 0.44. UV (MeOH): 209 (40800), 270 (sh, 6500), 276 (7200), 294 (6200), 304 (sh, 4600). ^{1}H-NMR ((D$_6$)DMSO): 2.43 (*ddd*, *J* = 4.6, 6.5, 13.2, $H_α$–C(2′)); 2.72 (‘*q*’, *J* = 6.6, $H_β$–C(2′)); 3.60 (*m*, 2 H–C(5′)); 3.97 (*m*, H–C(4′)); 4.49 (*m*, H–C(3′)); 5.03 (*t*, *J* = 5.6, OH–C(5′)); 5.36 (*d*, *J* = 4.3, OH–C(3′)); 6.44 (‘*t*’, *J* = 6.0, H–C(1′)); 7.07 (*m*, H–C(5)); 7.28 (*m*, H–C(6)); 7.64 (*d*, *J* = 8.8, H–C(7)); 7.73 (*d*, *J* = 8.4, H–C(4)); 8.61 (*s*, H–C(3)). Anal. calc. for $C_{12}H_{14}N_2O_3$: C 61.53, H 6.02, N 11.96; found: C 61.64, H 6.09, N 11.97.

*4-Nitro-1*H*-indazole* (**4b**) was synthesized as described in [31]. ^{1}H-NMR ((D$_6$)DMSO): 7.59 ('*t*', *J* = 8.2, H–C(6)); 8.10 (*d*, *J* = 8.2, H–C(5) or H–C(7)); 8.14 (*d*, *J* = 8.2, H–C(5) or H–C(7)); 8.53 (*d*, *J* = 0.8, H–C(3)); NH not observed.

Glycosylation of **4b** *with* **5**. Glycosylation of **4b** (2.0 g, 12.26 mmol) was performed as described for **4a**, using **5** (5.0 g, 12.86 mmol), powdered KOH (1.71 g, 30.5 mmol), TDA-1 (356 mg, 1.2 mmol), and anh. MeCN (350 ml). Purification by FC (50 × 5.5 cm, *C*) gave **6b** and **7b**.

*1-[2'-Deoxy-3',5'-bis-*O*-(4-methylbenzoyl)-β-*D-erythro-*pentofuranosyl]-4-nitro-1*H*-indazole* (**6b**). From the zone with R_f 0.35, **6b** was obtained as a yellow oil. Upon addition of light petroleum (50 ml), yellowish needles (2.15 g, 34%) were formed. M.p. 140–141°. UV (MeOH): 239 (42100), 274 (sh, 3100), 283 (3100), 343 (sh, 6200), 338 (6600). ^{1}H-NMR ((D$_6$)DMSO): 2.36, 2.41 (2*s*, 2 CH$_3$); 2.81 (*m*, H$_\alpha$–C(2')); 3.46 (*m*, H$_\beta$–C(2')); 4.34 (*dd*, *J* = 5.1, 11.7, 1 H–C(5')); 4.48–4.61 (*m*, H–C(4'), 1 H–C(5')); 5.88 (*m*, H–C(3')); 6.99 ('*t*', *J* = 5.9, H–C(1')); 7.27, 7.37 (2*d*, *J* = 8.2, 4 arom. H); 7.68 ('*t*', *J* = 8.1, H–C(6)); 7.76, 7.97 (2*d*, *J* = 8.1, 4 arom. H); 8.19 (*d*, *J* = 8.1, H–C(5)); 8.41 (*d*, *J* = 8.1, H–C(7)); 8.59 (*s*, H–C(3)). Anal. calc. for $C_{28}H_{25}N_3O_7$: C 65.24, H 4.89, N 8.15; found: C 65.36, H 4.91, N 8.13.

*2-[2'-Deoxy-3',5'-bis-*O*-(4-methylbenzoyl)-β-*D-erythro-*pentofuranosyl]-4-nitro-2*H*-indazole* (**7b**). The zone with R_f 0.45 contained **7b**. Trituration with light petroleum gave yellow crystals (2.15 g, 34%). M.p. 92–93°. UV (MeOH): 239 (38500), 282 (3300), 311 (5100), 338 (4700), 363 (6100). ^{1}H-NMR ((D$_6$)DMSO): 2.34, 2.41 (2*s*, 2 CH$_3$); 2.91 (*m*, H$_\alpha$–C(2')); 3.77 (*m*, H$_\beta$–C(2')); 4.49 (*dd*, *J* = 4.4, 11.0, 1 H–C(5')); 4.62–4.73 (*m*, H–C(4'), 1 H–C(5')); 5.90 (*m*, H–C(3')); 6.83 ('*t*', *J* = 5.8, H–C(1')); 7.22, 7.37 (2*d*, *J* = 8.1, 8 arom. H); 7.53 (*dd*, *J* = 7.6, 8.6, H–C(6)); 8.20 (*d*, *J* = 7.6, H–C(7)); 9.07 (*s*, H–C(3)). Anal. calc. for $C_{28}H_{25}N_3O_7$: C 65.24, H 4.89, N 8.15; found: C 65.37, H 4.92, N 8.21.

*1-(2'-Deoxy-β-*D-erythro-*pentofuranosyl)-4-nitro-1*H*-indazole* (**8b**). Compound **8b** was prepared from **6b** (2.0 g, 3.88 mmol) as described for **8a**, using MeOH (450 ml) and 1M NaOMe/MeOH (7.8 ml). Yellowish crystals (810 mg, 75%) were obtained upon crystallization from MeOH. M.p. 139–140°. TLC (*D*): R_f 0.25. UV (MeOH): 203 (18300), 214 (sh, 9200), 234 (11100), 338 (6700), 342 (sh, 6500). ^{1}H-NMR ((D$_6$)DMSO): 2.39 (*ddd*, *J* = 4.5, 6.7, 13.2, H$_\alpha$–C(2')); 2.98 ('*q*', *J* = 6.0, 13.2, H$_\beta$–C(2')); 3.35 ('*q*', *J* = 5.8, 11.4, 1 H–C(5')); 3.53 ('*q*', *J* = 5.4, 11.4, 1 H–C(5')); 3.90 (*m*, H–C(4')); 4.52 (*m*, H–C(3')); 4.77 (*t*, *J* = 5.6, OH–C(5')); 5.38 (*d*, *J* = 4.3, OH–C(3')); 6.73 ('*t*', *J* = 6.1, H–C(1')); 7.65 ('*t*', *J* = 8.0, H–C(6)); 8.16 (*d*, *J* = 8.0, H–C(5)); 8.36 (*d*, *J* = 8.0, H–C(7)); 8.57 (*s*, H–C(3)). Anal. calc. for $C_{12}H_{13}N_3O_5$: C 51.61, H 4.69, N 15.05; found: C 51.62, H 4.81, N 15.01.

*2-(2'-Deoxy-β-*D-erythro-*pentofuranosyl)-4-nitro-2*H*-indazole* (**9b**). Compound **9b** was prepared from **7b** (2.0 g, 3.88 mmol) as described for **8b**: yellowish oil (823 mg, 76%). TLC (*D*): R_f 0.25. UV (MeOH): 203 (31200), 230 (8500), 312 (5200), 361 (6400). ^{1}H-NMR ((D$_6$)DMSO): 2.47 (*m*, H$_\alpha$–C(2')); 2.73 (*m*, H$_\beta$–C(2')); 3.61 (*m*, 2 H–C(5')); 3.98 (*m*, H–C(4')); 4.49 (*m*, H–C(3')); 4.99 (*t*, *J* = 5.4, OH–C(5')); 5.40 (*d*, *J* = 4.4, OH–C(3')); 6.55 (*dd*, *J* = 5.5, 6.3, H–C(1')); 7.53 ('*t*', *J* = 7.9, H–C(6)); 8.22 (*d*, *J* = 7.9, H–C(5), H–C(7)); 9.12 (*s*, H–C(3)). Anal. calc. for $C_{12}H_{13}N_3O_5$: C 51.61, H 4.69, N 15.05; found: C 51.87, H 4.84, N 14.86.

*4-Amino-1-(2'-deoxy-β-*D-erythro-*pentofuranosyl)-1*H*-indazole* (**1**). Compound **8b** (250 mg, 0.90 mmol) in EtOH (50 ml) was hydrogenated for 4 h in the presence of 10% Pd/C (50 mg) at r.t./1 atm. The catalyst was filtered off and washed with EtOH. The solvent was evaporated and the residue applied to FC (3.5 × 25 cm, *D*). From the main zone, a colorless oil was obtained crystallizing upon storage (134 mg, 60%). M.p. 131–133°. TLC (*D*): R_f 0.12. UV (MeOH): 207 (sh, 21600), 214 (23700), 225 (sh, 17100), 264 (4900), 313 (8800). ^{1}H-NMR ((D$_6$)DMSO): 2.26 (*ddd*, *J* = 4.2, 6.7, 13.1, H$_\alpha$–C(2')); 2.91 ('*q*', *J* = 6.4, H$_\beta$–C(2')); 3.35 (*m*, 1 H–C(5')); 3.51 (*m*, 1 H–C(5')); 3.83 (*m*, H–C(4')); 4.47 (*m*, H–C(3')); 4.76 (*t*, *J* = 5.6, OH–C(5')); 5.28 (*d*, *J* = 4.3, OH–C(3')); 5.82 (br. *s*, NH$_2$); 6.22 (*d*, *J* = 7.5, H–C(5)); 6.44 ('*t*', *J* = 6.3, H–C(1')); 6.79 (*d*, *J* = 8.2, H–C(7)); 7.07 ('*t*', *J* = 7.8, H–C(6)); 8.19 (*s*, H–C(3)). Anal. calc. for $C_{12}H_{15}N_3O_3$: C 57.82, H 6.07, N 16.86; found: C 57.99, H 6.30, N 16.70.

*4-Amino-2-(2'-deoxy-β-*D-erythro-*pentofuranosyl)-2*H*-indazole* (**2**). Compound **9b** (250 mg, 0.90 mmol) was hydrogenated as described for **1**. FC (2.5 × 10 cm, *D*) yielded a colorless oil (61 mg, 27%), which crystallized upon storage. TLC (*D*): R_f 0.08. UV (MeOH): 223 (25800), 268 (sh, 2100), 281 (sh, 1900), 325 (5300). ^{1}H-NMR ((D$_6$)DMSO): 2.36 (*m*, H$_\alpha$–C(2')); 2.67 (*m*, H$_\beta$–C(2')); 3.53 (*m*, 2 H–C(5')); 3.91 (*m*, H–C(4')); 4.43 (*m*, H–C(3')); 4.97 (*t*, *J* = 5.6, OH–C(5')); 5.29 (*d*, *J* = 4.3, OH–C(3')); 5.59 (br. *s*, NH$_2$); 6.00 (*d*, *J* = 6.9, H–C(5)); 6.31 ('*t*', *J* = 6.0, H–C(1')); 6.71 (*d*, *J* = 8.2, H–C(7)); 6.94 (*m*, H–C(6)); 8.48 (*s*, H–C(3)). Anal. calc. for $C_{12}H_{15}N_3O_3$: C 57.82, H 6.07, N 16.86; found: C 57.75, H 6.09, N 16.79.

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