Carbohydrate Research, 93 (1981) 19–34
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

3-β-D-RIBOFURANOSYLINDOLES (INDOLE *C*-NUCLEOSIDES)*

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(Received September 23rd, 1980; accepted for publication, December 1st, 1980)

ABSTRACT

The reaction of indole with a glycosyl halide containing a non-participating group at position 2 in the presence of silver oxide and molecular sieve in dry benzene yielded an *O*-substituted 3-glycosylindole (indole *C*-nucleoside). 2,3,4,6-Tetra-*O*-benzyl-D-glucopyranosyl bromide and 6-nitroindole gave anomeric per-*O*-benzylated 3-D-glucopyranosyl-6-nitroindoles; from 2,3,5-tri-*O*-benzyl-D-ribofuranosyl bromide and 6-nitroindole, anomeric per-*O*-benzylated 6-nitro-3-D-ribofuranosylindoles were obtained. Starting from 2,3-*O*-isopropylidene-5-*O*-*p*-nitrobenzoyl-D-ribofuranosyl bromide, the individual α and β anomers of the *O*-protected 3-D-ribofuranosyl derivatives of indole, 5-bromoindole, 5-nitroindole, or 6-nitroindole were synthesised. Treatment of the α anomers with acid gave the corresponding β anomers. After *O*-deprotection, 3-β-D-ribofuranosyl derivatives of 5- and 6-nitroindole were obtained. 2,3-Di-*O*-*p*-toluoyl-D-ribofuranosyl chloride and 6-nitroindole gave the anomeric 1-(2-deoxy-D-*erythro*-pentofuranosyl)-6-nitroindoles and 3-(2-deoxy-D-*erythro*-pentofuranosyl)-6-nitroindoles.

INTRODUCTION

In contrast to *N*-indole nucleosides, which have been widely studied, there is no general procedure for the synthesis of 3-nucleosides of indoles. Indole *C*-nucleosides are model compounds in the synthesis of 9-nucleosides of 9-deazapurines.

We have described[2,3] the reaction of indoles with glycosyl halides containing a participating 2-acyloxy group. Indole or 5- or 6-nitroindole and 2,3,4-tri-*O*-acetyl-β-L-arabinopyranosyl bromide in boiling benzene in the presence of silver oxide and molecular sieve yielded a mixture of per-*O*-acetylated 1-α-L-arabinopyranosylindole, 3-α-L-arabinopyranosylindole (the first indole *C*-nucleoside), and 1,2-*O*-[1-(indol-1-yl)ethylidene]-β-L-arabinopyranose, or the corresponding 5- or 6-nitro derivatives. Under similar conditions, tetra-*O*-acetyl-α-D-glucopyranosyl bromide or 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide produced only 1,2-*O*-(indol-1-yl)- or 1,2-*O*-(indol-3-yl)-alkylidene derivatives (**1** or **2**). The absence of *N*- or *C*-nucleosides from the

*Previous communication, see ref. 1.

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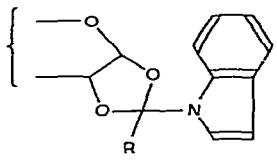
products of these reactions can be explained by the steric effect of CH_2OAc or CH_2OBz substituents of the ribofuranose or glucopyranose derivatives.



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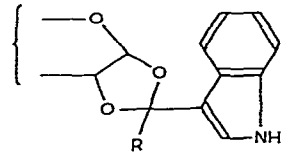

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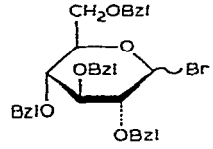
Therefore, we concluded that for the preparation of *C*- or *N*-glycosylindoles by this method it is necessary to use glycosyl halides that have a non-participating group at position 2 and therefore cannot form 1,2-indolylalkylidene derivatives.

RESULTS AND DISCUSSION

We now describe the interaction of indoles in boiling benzene in the presence of silver oxide and molecular sieve with 2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl bromide[4] (**3**), 2,3,5-tri-*O*-benzyl-D-ribofuranosyl bromide[5] (**4**), 2,3-*O*-isopropylidene-5-*O*-trityl-D-ribofuranosyl chloride[6] (**5**), 2,3-*O*-isopropylidene-5-*O*-*p*-nitrobenzoyl-D-ribofuranosyl bromide[7] (**6**), and 2-deoxy-3,5-di-*O*-*p*-toluoyl-D-*erythro*-pentofuranosyl chloride[8] (**7**).



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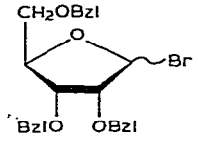

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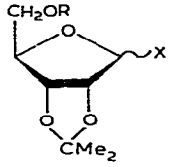
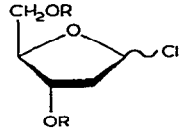


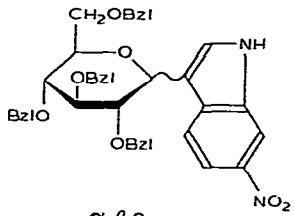
5 X = Cl, R = Tr
6 X = Br, R = *p*-$NO_2C_6H_4CO$



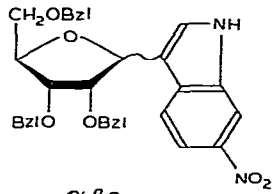
7 R = *p*-MeC_6H_4CO

6-Nitroindole and **3** produced an anomeric mixture (17% yield) of per-*O*-benzylated 3-D-glucopyranosyl-6-nitroindoles (**8**). Similarly, 6-nitroindole and **4** yielded the anomeric mixture **9** (16% yield). Attempts to isolate the individual anomers from these mixtures were unsuccessful. In the p.m.r. spectra of the mixtures **8** or **9**, there were NH signals, but indole 3-H signals were absent. The p.m.r. spectra demonstrate the presence of two anomers for **8** and for **9**. The i.r. spectra contained bands at 3400 cm^{-1} characteristic of NH-stretching. Per-*O*-benzylated *N*-nucleosides of 6-nitroindole were absent from the reaction mixtures.

The rather low yields of the *C*-nucleosides prompted a study of other glycosyl halides. 2,3-*O*-Isopropylidene-5-*O*-trityl-D-ribofuranosyl chloride (**5**) has been used for the preparation of *C*-nucleosides[9]. However, in the reaction with 6-nitroindole,



αβ 8



αβ 9

5 decomposed and no indole–sugar derivative was isolated. Similarly, no indole nucleosides were obtained by the reaction of 5 with 5- or 6-nitroindole in dry acetonitrile at room temperature in the presence of silver oxide and molecular sieve, under the conditions successfully used for the condensation of 5 with silver acetylide or silver ethyl propiolate[10].

2,3-*O*-Isopropylidene-5-*O*-*p*-nitrobenzoyl-D-ribofuranosyl bromide (**6**) was found to be the most suitable glycosylating agent for the synthesis of indole *C*-nucleosides. The reaction of **6** with indole, 5- or 6-nitroindole, or 5-bromoindole gave αβ-mixtures of the 3-(2,3-*O*-isopropylidene-5-*O*-*p*-nitrobenzoyl)-D-ribofuranosylindoles (**10–17**) in yields of 38–47%. The compounds were isolated by p.l.c. In all cases, α anomers were preponderant (for **15** and **14**, the αβ-ratio was 3 : 1; for the other pairs of isomers, it was ~4 : 1). Glycosylation with 2,3-*O*-isopropylideneribose derivatives yields mainly α-nucleosides[11,12], probably because of participation by

TABLE I

DATA FOR NEW INDOLE DERIVATIVES

Compound	*M.p.*[a] *(degrees)*	$[\alpha]_D^{20}$ (c, $CHCl_3$) *(degrees)*	*Found* (%)			*Calc.* (%)			*Formula*
			C	*H*	*N*	*C*	*H*	*N*	
10[b]	a	−17.0 (0.75)							
11[b]	a	−20.0 (1.0)	61.3	5.0	6.6	61.1	5.2	6.2	$C_{23}H_{22}N_2O_7 \cdot 0.75\ H_2O$
12[b]	a	−21.5 (1.0)							
13[b]	a	−12.0 (1.0)	51.3	4.2	5.6	51.6	4.3	5.2	$C_{23}H_{21}BrN_2O_7 \cdot H_2O$
14	a	−27.6 (0.5)	57.0	4.4	8.7	57.1	4.4	8.7	$C_{23}H_{21}N_3O_9$
15	a	−16.8 (0.5)	56.1	4.7	8.5	56.1	4.5	8.5	$C_{23}H_{21}N_3O_9 \cdot 0.5\ H_2O$
16[b]	a	−15.0 (1.0)							
17	a	+3.5 (1.0)	55.2	4.4	8.8	55.1	4.6	8.4	$C_{23}H_{21}N_3O_9 \cdot H_2O$
19	a		52.6	4.1	9.2	52.7	4.5	9.6	$C_{20}H_{17}N_3O_9 \cdot 0.75\ H_2O$
20	152–153[c]	−33.0 (1.0[c])	51.4	5.2	9.3	51.5	5.0	9.2	$C_{13}H_{14}N_2O_6 \cdot 0.5\ H_2O$
21	a	−10.0 (1.0[c])	50.7	5.5	9.1	50.7	5.1	9.1	$C_{13}H_{14}N_2O_6 \cdot 0.75\ H_2O$
22	155–156[c]	−16.4 (1.0)	54.0	4.1	7.9	54.0	4.2	7.3	$C_{26}H_{23}N_3O_{12} \cdot 0.5\ H_2O$
24[b]	a		53.5	4.8		53.5	4.9		$C_{21}H_{22}N_2O_{10} \cdot 0.5\ H_2O$
34(35)[b]	119–120[c]	+13.0 (0.5[c])	54.3	4.4	7.5	54.6	4.7	7.1	$C_{27}H_{25}N_3O_{11} \cdot 1.5\ H_2O$
38			67.6	5.1	5.5	67.7	5.1	5.4	$C_{29}H_{26}N_2O_7$
39[b]			53.8	5.6		53.6	5.4		$C_{13}H_{14}N_2O_5 \cdot 0.75\ H_2O$
40			53.6	5.6		53.6	5.4		$C_{13}H_{14}N_2O_5 \cdot 0.75\ H_2O$

[a]a, Amorphous. [b]Structure confirmed by mass spectrometry. [c]Methanol.

TABLE II

P.M.R. DATA[a] FOR THE 3-β-D-RIBOFURANOSYL DERIVATIVES OF INDOLE OR 5-BROMOINDOLE

Compound (configuration)	*Chemical shifts (p.p.m., J in Hz)*													
	Indole protons						*Sugar protons*						*BzNO₂*	*CMe₂ (Δδ)*
	NH	*H-7*	*H-6*	*H-5*	*H-4*	*H-2*	*H-1′* ($J_{1',2'}$)	*H-2′*	*H-3′*	*H-4′*	*H-5′*	*H-5″*		
10 (β)	8.40					6.95	5.29 (4.2)	5.10				4.30	8.19	1.65 1.37 (0.28)
11 (α)	8.20					7.08	5.39 (3.2)	5.0				4.35	8.22	1.55 1.34 (0.21)
12 (β)	8.36		7.32[b]		7.80	[b]	5.16 (4.0)	5.0	4.80	4.70		4.46	[b]	1.65 1.38 (0.27)
13 (α)	8.41	7.15	7.32		7.87	7.11	5.30 (3.2)	5.0				4.28	8.21	1.56 1.34 (0.22)

[a]$CDCl_3$, 25°. [b]Overlapping signals.

TABLE III

P.M.R. DATA[a] FOR THE 5-NITROINDOLE DERIVATIVES

Compound (configuration)	*Chemical shifts (p.p.m., J in Hz)*													
	Indole protons					*Sugar protons*						*$BzNO_2$*	*CMe_2 ($\Delta\delta$)*	*OAc (NAc)*
	NH	*H-4*	*H-6*	*H-2*	*H-7*	*H-1′ ($J_{1',2'}$)*	*H-2′*	*H-3′*	*H-4′*	*H-5′*	*H-5″*			
16 (β)	9.21	8.61	8.00	7.40	7.34	5.26 (3.2)	5.0 —— 4.80		4.80 —— 4.30			8.14	1.66 1.39 (0.27)	
17 (α)	8.91	8.76	8.04	7.48	7.35	5.39 (3.2)	5.04 —— 4.30					8.23	1.58 1.34 (0.24)	
19[b]		8.68	7.93	7.42	7.34	5.15 (4.4)	4.90 —— 4.20					8.30–8.10		
21[b]		8.76	8.01	7.51	7.43	5.08 (6.0)	4.30 —— 3.40							
23	8.96	8.69	8.08	7.50—7.30		5.74 —— 5.36			4.80 —— 4.40			8.18		2.18 2.12
25	9.28	8.72	8.08	7.41	7.36	← 5.32 →			← 4.41 →					2.16 2.13 2.09 (2.67)
26		8.65	8.23	7.68	8.56	5.48 —— 5.20			← 4.42 →					2.16 2.12 } 3 OAc

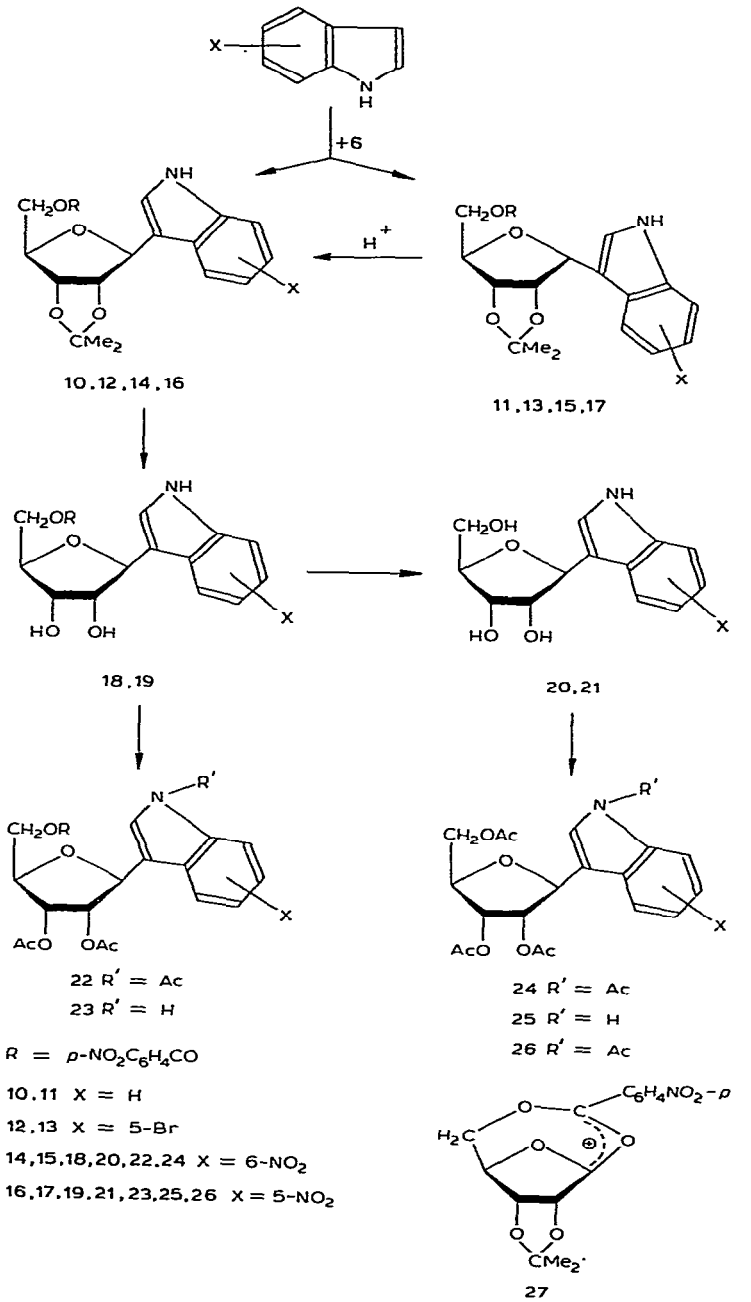
[a]$CDCl_3$ at 25°. [b]In CD_3OD.

TABLE IV

P.M.R. DATA (25°) FOR THE 6-NITROINDOLE DERIVATIVES

Compound (configuration)	*Chemical shifts (p.p.m., J in Hz)*													
	Indole protons					*Sugar protons*						$BzNO_2$	CMe_2 ($\Delta\delta$)	*OAc (NAc)*
	NH	*H-7*	*H-5*	*H-4*	*H-2*	*H-1′* ($J_{1',2'}$)	*H-2′*	*H-3′*	*H-4′*	*H-5′*	*H-5″*			
14[b] (β)	9.32	[a]	7.81	7.61	7.46	5.25[c]	4.96				4.40	8.15[a]	1.67 1.42 (0.25)	
15[b] (α)	9.24	[a]	7.94	7.71	7.59	5.38 (3.0)	5.08				4.32	8.18[a]	1.55 1.35 (0.20)	
18[c]	8.44				7.64	5.40					4.00	8.28		
20[d]		8.32	7.90[a]	[a]	7.67	5.04 (6.2)	4.24				3.60			
22[b]		9.20	8.05	7.84	7.68	5.56		5.28	4.96		4.48	8.24		2.16 2.13 (2.60) 2.13 2.11 (2.69) } 3 OAc
24[b]		9.32	8.17	7.81	7.34	← 5.30 →			← 4.42 →					

[a]Overlapping signals. [b]In $CDCl_3$. [c]In Me_2SO. [d]In CD_3OD. [e]Halfwidth, ~6 Hz.

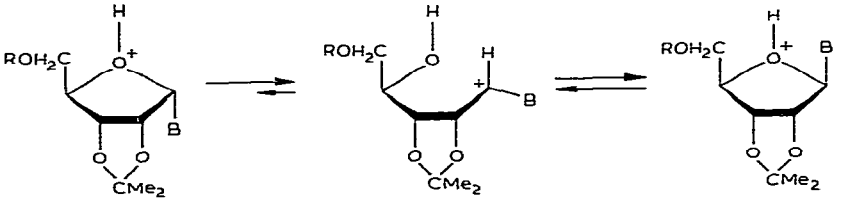


the 5′-*O*-acyloxy group and the formation of the intermediate structure **27**. Some properties of the products are given in Table I, and the p.m.r. data in Tables II–IV.

The p.m.r. data supported the assigned structures of the anomeric nucleosides. There were NH signals in the spectra of **13–17**; for the compounds **10–12**, the signal

was overlapped by those for the aromatic protons. There were no H-3 doublets at δ 6.0–7.0 in these spectra. The i.r. spectra contained characteristic NH-stretching absorption at 3400 cm^{-1}.

The assignment of anomeric configuration was based upon the well-known, upfield shifts of the H-1′ signals for β-nucleosides compared with the α-nucleosides[13]. Usually, $J_{1',2'}$ for β-nucleosides is smaller than for the corresponding α-nucleosides[13], but this rule failed with the isomers described herein, as it did for the nucleosides of pyrrolo(2,3-*d*)pyrimidines[14] and benzimidazoles[15]. The criterion[16] for the determination of configuration of 2,3-*O*-isopropylidene derivatives of nucleosides ($\Delta\delta_{CH_3} > 0.15$ for the β anomer and $\Delta\delta_{CH_3} < 0.15$ for the α anomer) should be limited to ribofuranosyl compounds containing no 5′-substituent. However, for the pairs of anomeric *C*-nucleosides described herein, $\Delta\delta_{CH_3}$ for the α anomer was smaller than for the corresponding β anomer. This trend has also been described for other 5′-substituted *C*-nucleosides[17]. The H-4 signal for the α anomer (**11**, **13**, **15**, or **17**) was at lower field than that for the corresponding β anomer (**10**, **12**, **14**, or **16**). The Me signals for the α anomers were more shielded than for the corresponding β anomers. To remove the *O*-isopropylidene group, the action of acids on the nucleosides **10–17** was studied under different conditions. In acid media, protonation of the oxygen atom of the ribofuranose ring or the oxygen atoms of the dioxolane ring can occur. For the former (**28** or **30**), opening of the ribofuranose ring (**29**) can occur, and subsequent cyclisation yields the thermodynamically more stable isomer (ribopyranose isomers are not formed, because position 5′ is blocked). Protonation of the dioxolane ring (for example, **31**) is followed by cleavage of the ring and formation of the oxocarbonium ions (**32** or **33**) with subsequent loss of the isopropylidene group.



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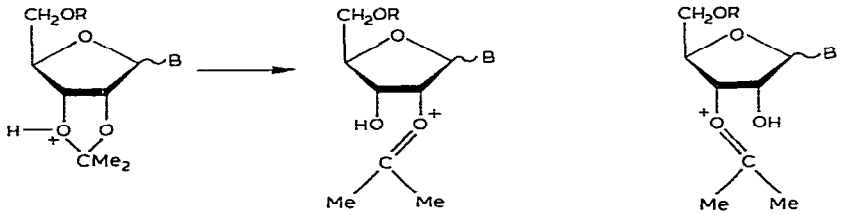
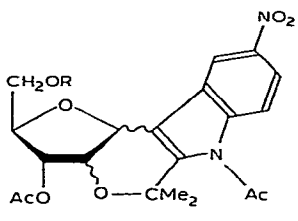


31 32 33

Due to the electron-donor properties of the indole heterocycle, protonation of the ribofuranose ring-oxygen atom and therefore anomerisation easily occur. The action of picric acid on the α anomers **11** or **13** in alcohol or 1,4-dioxane at room temperature afforded the corresponding β anomers **10** or **12**. Attempts to remove the isopropylidene group by the action of hydrogen chloride, CF_3COOH, or Dowex (H^+) resin in various solvents caused extensive decomposition.

The nucleosides **14** or **15**, or a mixture thereof, in M aqueous, methanolic hydrochloric acid (10M HCl–methanol, 1 : 10) yielded 6-nitro-3-(5-*O*-*p*-nitrobenzoyl-β-D-ribofuranosyl)indole (**18**). 5-Nitro-3-(5-*O*-*p*-nitrobenzoyl-β-D-ribofuranosyl)indole (**19**) was obtained by treatment of **16** or **17** or **16** + **17** with 90% CF_3COOH.

The action of M aqueous, methanolic hydrogen chloride on **17** gave a new compound, acetylation of which afforded an *O*-acetyl derivative for which the structure **34** or **35** is proposed. Intermediates for these products would be of the type **32** or **33**, since attack of the oxocarbonium ion on C-2 of the indole system would yield a dihydropyran derivative (previous α→β anomerisation cannot be excluded). Compound **36** has been obtained[18] by the action of acid on 1-(2,3-*O*-isopropylidene-α-D-ribofuranosyl)pyrrole. The structure **34** (**35**) was supported by mass-spectrometric data. Peaks corresponding to *m/z* values of M* (567), $M^+ - OCMe_2$ (509), B + 30 (232), and B (202) are diagnostic.



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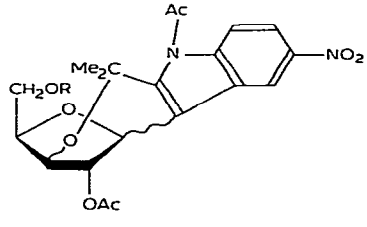

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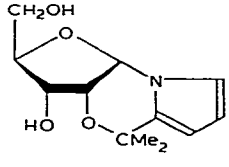


36

The p.m.r. spectrum of **34** (**35**) in $CDCl_3$ at 25°, which contained no signals for pyrrole protons, contained signals at δ 7.65 and 6.68 (2 s, H-1′,2′), 5.88 (bd, splitting 6.8 Hz, H-3′), 5.70–5.50 (m, H-4′), 4.84 (m, $J_{4',5'a}$ 2.8, $J_{5'a,5'b}$ 12.4 Hz, H-5′a), 4.53 (m, $J_{4',5'b}$ 5.8 Hz, H-5′b), 2.66 (NAc), 2.15 (OAc), 2.13 and 2.08 (CMe_2). The $J_{1',2'}$ and $J_{2',3'}$ values are close to zero, indicating that the dihedral angles for H-1′/H-2′ and H-2′/H-3′ are close to 90°. Dreiding models demonstrate that these dihedral angles are close to 90° for **35** having the β-D-*xylo* configuration. However, a reasonable mechanism of epimerisation at C-3′, leading to **35** with the β-D-*xylo* configuration, cannot be proposed. Therefore, the α-D-*ribo* structure **34** seems to be the most probable.

The unsubstituted *C*-nucleosides **20** and **21** were prepared by the action of methanolic ammonia on **18** and **19**, respectively, and were homogeneous by h.p.l.c. in 30% methanol (retention times of 23.92 and 23.33 min, respectively).

Acetylation of the 6-nitro derivative **18** gave the *N*-acetyl-2,3-di-*O*-acetyl

TABLE V

C.D. DATA FOR THE 3-D-RIBOFURANOSYLINDOLES

Compound (configuration)	*Major maxima* λ, *nm* ($\theta \times 10^{-3}$)	*Minor maxima*
10 (β)	220 (−15.8)	255 (+2.2)
11 (α)	254 (+6.85)	285 (−1.45), 293 (−0.5)
12 (β)	228 (−23.2)	280 (+2.55)
13 (α)	255 (+7.95)	280 (−0.5), 287 (+0.15) 296 (+0.85)
14 (β)	272 (−4.3)	228 (+0.8), 340 (+0.4) 245 (−1.1)
15 (α)	262 (+4.8)	245 (−1.75), 320 (+1.35)
16 (β)	255 (−3.75), 275 (+4.0)	266 (+0.75), 360 (−0.8)
17 (α)	245 (+4.0), 276 (−1.5) 308 (+2.4)	350 (−0.8)
20 (β)	260 (−1.65)	230 (+0.55), 290 (+0.39)
34(35)	230 (+6.27), 260 (−5.24) 280 (+3.37)	350 (−1.03)

derivative **22**; likewise, the 5-nitronucleoside afforded the di-*O*-acetyl derivative **23**. Acetylation of **20** yielded the *N*-acetyl-2,3,5-tri-*O*-acetyl compound **24**, and the 5-nitro isomer **21** gave a mixture of tri- (**25**) and tetra-acetyl (**26**) derivatives. Therefore, *N*-acetylation occurs only for nitroindole *C*-nucleosides, 6-nitroindole derivatives affording *N*-acetyl compounds in yields higher than those from 5-nitroindole deriva-

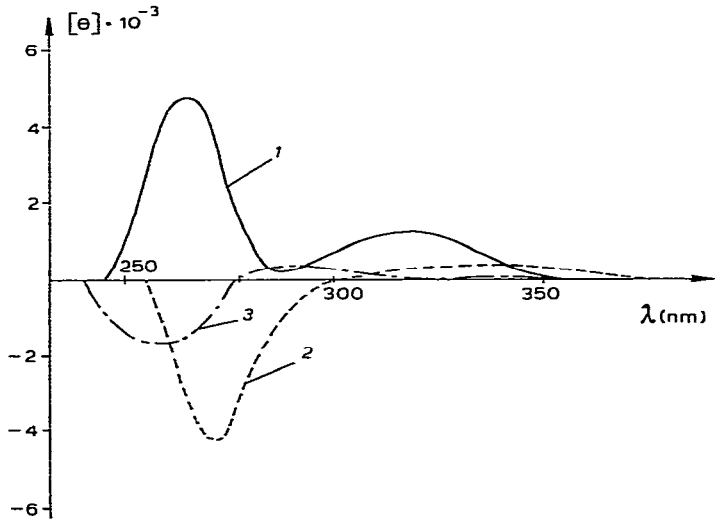


Fig. 1. C.d. spectra in ethanol: **1**, 3-(2,3-*O*-isopropylidene-5-*O*-*p*-nitrobenzoyl-α-D-ribofuranosyl)-6-nitroindole (**15**); **2**, 3-(2,3-*O*-isopropylidene-5-*O*-*p*-nitrobenzoyl-β-D-ribofuranosyl)-6-nitroindole (**14**); **3**, 6-nitro-3-β-D-ribofuranosylindole (**20**).

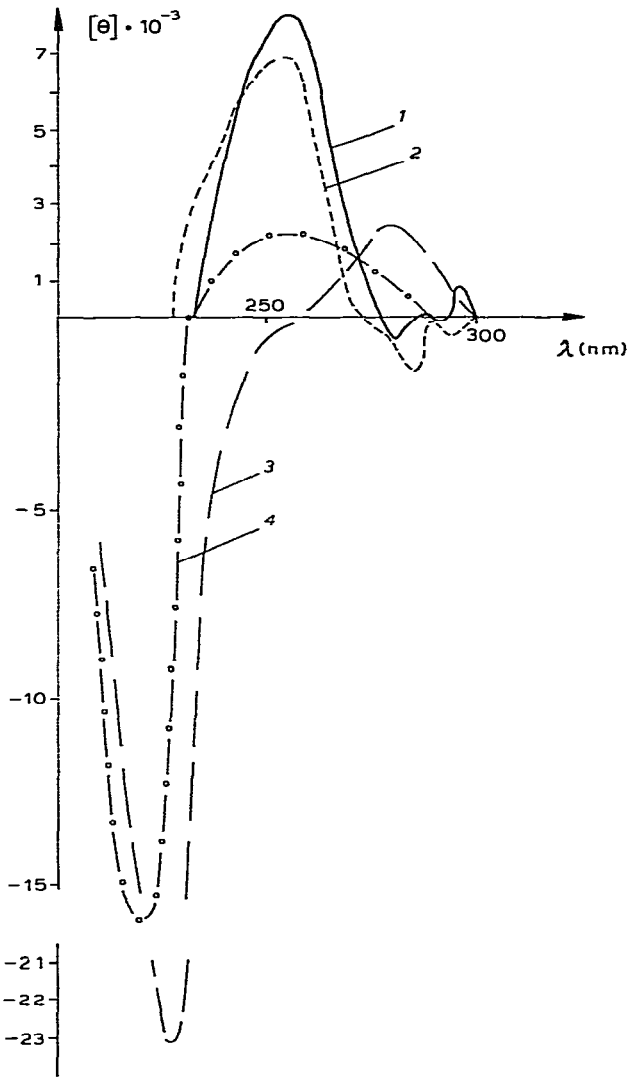


Fig. 2. C.d. spectra in ethanol: **1**, 5-bromo-3-(2,3-*O*-isopropylidene-5-*O*-*p*-nitrobenzoyl-α-D-ribofuranosyl)indole (**13**); **2**, 3-(2,3-*O*-isopropylidene-5-*O*-*p*-nitrobenzoyl-α-D-ribofuranosyl)indole (**11**); **3**, 5-bromo-3-(2,3-*O*-isopropylidene-5-*O*-*p*-nitrobenzoyl-β-D-ribofuranosyl)indole (**12**); **4**, 3-(2,3-*O*-isopropylidene-5-*O*-*p*-nitrobenzoyl-β-D-ribofuranosyl)indole (**10**).

tives. Similarly, acetylation of the previously described 3-α-L-arabinopyranosyl-6-nitroindole[2,3] gave the *N*-acetyl-2,3,4-tri-*O*-acetyl derivative, and 3-α-L-arabinopyranosyl-5-nitroindole gave only the 2,3,4-triacetate. U.v. data indicate 5- and 6-nitroindoles to be more acidic (pK_a 15–16) than indole, the pK_a of 6-nitroindole being 0.5 smaller than the pK_a of 5-nitroindole. Thus, the concentration of the corresponding anions of 3-ribofuranosyl-nitroindoles in the presence of bases will be higher for the 6-nitro derivative than for the 5-nitro derivative, and this is the

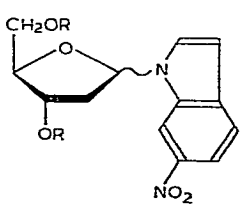
reason for formation of the *N*-acetyl derivative. The p.m.r. spectra of the per-*O*-acetylated nucleosides **22–26** contain signals for AcO-2′ at $\delta > 2.09$, whereas per-*O*-acetylated α-nucleosides usually have[19] this resonance at $\delta < 1.95$. The c.d. spectra of the *C*-nucleosides are shown in Table V. The isopropylidene derivatives of α-nucleosides (**11**, **13**, **15**, or **17**) showed positive maxima at 230–270 nm, whereas the corresponding β anomers (**10**, **12**, **14**, or **16**) had negative maxima in this region. The position of the strongest maxima for the α anomers of nitroindole nucleosides is shifted to shorter wavelengths by 10 nm compared with the corresponding β anomers (Table V, Fig. 1). A similar shift of the maxima was found in the c.d. spectra of the anomeric 5-fluoro-1-D-ribofuranosyluracils[20]. In the c.d. spectra of the α anomers of indole or bromoindole nucleosides (**11**, **13**), the strongest maxima are shifted to longer wavelengths by 27–37 nm compared with the corresponding β nucleosides **10** and **12** (Fig. 2). The c.d. spectrum of the unprotected nucleoside **20** is similar to that of the β nucleoside **14** (Fig. 1).

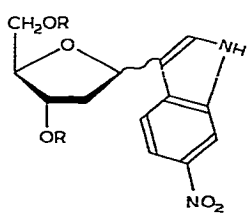
The structures of compounds **10–13**, **16**, **24**, **25**, and **26** were confirmed by high-resolution mass spectrometry. The mass spectra showed low-intensity peaks for molecular ions. Peaks corresponding to *m/z* values of $(B + 29)^+$ and $(S + 1)^+$ are diagnostic for *C*-nucleosides, whereas peaks $(B + 1)^+$ which are characteristic for *N*-nucleosides were absent.

Anomeric 1-(2-deoxy-3,5-di-*O*-toluoyl-D-*erythro*-pentofuranosyl)indoles have been recently obtained in the reaction of indole–sodium and 2-deoxy-3,5-di-*O*-toluoyl-D-*erythro*-pentofuranosyl chloride in liquid ammonia. It is noteworthy that *O*-deacetylation does not occur in this medium. After removal of protecting groups, the individual α and β anomers of 1-(2-deoxy-D-*erythro*-pentofuranosyl)indole were obtained[21].

The reaction of 6-nitroindole and 2-deoxy-3,5-di-*O*-*p*-toluoyl-D-*erythro*-pentofuranosyl chloride in the presence of silver oxide and molecular sieve in boiling benzene gave a mixture of anomeric, per-*O*-acylated 1- and 3-deoxynucleosides (**37** and **38**) which were isolated by p.l.c. in yields of 30% each. Zemplén deacylation then afforded the anomeric mixtures **39** and **40**. The anomers could not be separated by t.l.c.

The mixture **39** was identified as *N*-nucleosides by the presence of a doublet for H-3 in the p.m.r. spectrum. Such a doublet was absent from the p.m.r. spectrum





αβ-37 R = *p*-MeC$_6$H$_4$CO
αβ-39 R = H

αβ-38 R = *p*-MeC$_6$H$_4$CO
αβ-40 R = H

of **40**. The p.m.r. spectra also demonstrate the presence of two anomers. The i.r. spectrum of **38** contained absorption for NH at 3390 cm^{-1}.

The mass spectrum of **39** exhibited mass ions at *m/z* 278 (M^+), 162 $(B + 1)^+$, and 117 $(S)^+$ consistent with the proposed structure.

H.p.l.c. of the mixture **39** indicated the presence of two isomers in the ratio 5:6 with the retention times 16.87 and 17.24 min, respectively. Likewise, the ratio of anomeric *C*-deoxynucleosides **40** was shown to be 2:3, the retention times being 13.97 and 14.40 min [aqueous methanol gradient (20→80%; 25 min)].

EXPERIMENTAL

General. — P.m.r. spectra (internal Me_4Si) were recorded with a Jeol JNM-MH-100 instrument, and i.r. spectra (KBr) with a Perkin–Elmer 283 instrument. C.d. spectra were determined for solutions in ethanol with a Mark-III Dichrograph. U.v. spectra were recorded for solutions in ethanol with a Unicam SP-800 instrument. Optical rotations were determined with a Perkin–Elmer 241 polarimeter. Mass spectra (80 eV) were obtained with a Varian MAT-311A instrument; samples were introduced directly at 100–200° with an accelerating voltage of 3 kV and an emission current of 3 mA. H.p.l.c. was performed on a 1084 B Hewlett–Packard instrument (for **20** and **21**) and a Lirec instrument (Jobin Yvon) (for **39** and **40**) with a Li Chrosorb RP-18 "Hibar" column (250 × 4 mm; particle diameter, 10 μm) and an Altex detector (model 153) operated at 254 nm. T.l.c. was performed on Silufol UV254, and p.l.c. on silica gel LL_{254} 5/40 μm, with carbon tetrachloride–acetone mixtures *A*, 4:1; *B*, 2:1; and *C*, 1:2. Substances were eluted from silica gel by methanol.

Condensations of 6-nitroindole. — (*a*) *With 2,3,4,6-tetra-*O*-benzyl-*D*-glucopyranosyl bromide.* A mixture of 6-nitroindole (162 mg), Ag_2O (232 mg), dry benzene (50 ml), and molecular sieve (Wolfen Zeosorb 4Å Kugelform) was heated to boiling in a stream of nitrogen. Solvent (~10 ml) was evaporated and a solution of the glucosyl bromide (from 983 mg of 2,3,4,6-tetra-*O*-benzyl-1-*O*-*p*-nitrobenzoyl-D-glucopyranose) in dry benzene (20 ml) was added dropwise during 2.5 h with very slow distillation of solvent (~20 ml). The mixture was boiled for 20 h, cooled, and filtered, and the insoluble material was washed with benzene and chloroform. The combined filtrate and washings were concentrated, and the residue was dissolved in chloroform (2 ml) and subjected to p.l.c. (solvent *A*), to give **8** (R_F 0.38; 120 mg, 17%).

P.m.r. data ($CDCl_3$): δ 8.93 (s, NH), 8.19 (d, H-7), 7.85 (dd, H-5), 7.38 (d, H-4), 7.34–6.90 (m, H-2, Ph), 5.25 (bd, $J_{1',2'}$ <4 Hz, H-1′ of one isomer), and 5.04–3.44 (H-2′–H-6′, H-1′ of the other isomer, CH_2).

(*b*) *With 2,3,5-tri-*O*-benzyl-*D*-ribofuranosyl bromide.* 6-Nitroindole (162 mg) was treated with Ag_2O (232 mg) and the ribosyl bromide (from 725 mg of 2,3,5-tri-*O*-benzyl-1-*O*-*p*-nitrobenzoyl-D-ribofuranose), as described in (*a*). P.l.c. gave **9** (R_F 0.50; 90 mg, 16%).

P.m.r. data ($CDCl_3$): δ 8.89 (s, NH), 8.25 (d, H-7), 7.90 (dd, H-5), 7.45 (d,

H-4), 7.41–7.04 (m, H-2, Ph), 5.28 (bs, H-1′ of one isomer), and 4.64–3.24 (H-2′–5′; H-1′ of the other isomer).

*Condensations of 2,3-*O*-isopropylidene-5-*O*-*p*-nitrobenzoyl-*D*-ribofuranosyl bromide.* — (*a*) *With indole.* Indole (351 mg) was treated with Ag_2O (696 mg) and the ribosyl bromide (from 1464 mg of 2,3-*O*-isopropylidene-1,5-di-*O*-*p*-nitrobenzoyl-D-ribofuranose), as described in (*a*) for 6-nitroindole. P.l.c. gave **11** (R_F 0.22; 510 mg, 38%) and **10** (R_F 0.37; 120 mg, 9%). Mass spectrum of **11** or **10**: *m/z* 438 (M^+), 323 $(S + 1)^+$, and 155 $(B + 29)^+$.

(*b*) *With 5-bromoindole.* The reaction of 5-bromoindole (588 mg), Ag_2O (696 mg), and the ribosyl bromide (from 1464 mg of 2,3-*O*-isopropylidene-1,5-di-*O*-*p*-nitrobenzoyl-D-ribofuranose), as described above, yielded **13** (R_F 0.32; 500 mg, 31%) and **12** (R_F 0.39; 110 mg, 7%). Mass spectrum of **12** or **13**: *m/z* 516, 518 (M^+), 323 $(S + 1)^+$, 222, 224 $(B + 28)^+$, 223, and 225 $(B + 29)^+$.

(*c*) *With 6-nitroindole.* The reaction of 6-nitroindole (648 mg), Ag_2O (928 mg), and the ribosyl bromide (from 2928 mg of 2,3-*O*-isopropylidene-1,5-di-*O*-*p*-nitrobenzoyl-D-ribofuranose) gave, after p.l.c., **15** (R_F 0.10; 570 mg, 29%) and **14** (R_F 0.14; 170 mg, 9%).

(*d*) *With 5-nitroindole.* The reaction of 5-nitroindole (972 mg), Ag_2O (1392 mg), and the ribosyl bromide (from 2928 mg of 2,3-*O*-isopropylidene-1,5-di-*O*-*p*-nitrobenzoyl-D-ribofuranose), as described in (a), gave, after p.l.c., a mixture of **17** and **16** (R_F 0.20; 1370 mg, 46%). After three developments with solvent *A*, the α anomer **17** (R_F 0.16) and β anomer **16** (R_F 0.22) were isolated. Mass spectrum of **16**: *m/z* 483 (M^+), 323 $(S + 1)^+$, and 190 $(B + 29)^+$.

*Condensation of 6-nitroindole with 2-deoxy-3,5-di-*O*-p-toluoyl-*D*-erythro-pentofuranosyl chloride.* — 6-Nitroindole (569 mg) was treated with Ag_2O (696 mg) and 2-deoxy-3,5-di-*O*-*p*-toluoyl-D-*erythro*-pentofuranosyl chloride (1162 mg) in dry benzene (130 ml), as described in (*a*). Mixtures of anomers **37** (R_F 0.50; 470 mg, 30%) and **38** (R_F 0.31; 500 mg, 32%) were obtained.

*6-Nitro-3-(5-*O*-p-nitrobenzoyl-β-*D*-ribofuranosyl)indole* (**18**). — A suspension of **15** or **14** (330 mg) in a 1:10 mixture of 10M hydrochloric acid and methanol (15 ml) was stirred for 1.5 h at 20°. The green precipitate was filtered off and washed with water, to give **18** (270 mg, 89%).

*5-Nitro-3-(5-*O*-p-nitrobenzoyl-β-*D*-ribofuranosyl)indole* (**19**). — A solution of **17** or **16** (250 mg) in 90% CF_3COOH (10 ml) was kept at 20° for 1 h and then concentrated, and the residue was subjected to p.l.c. (solvent *B*), to give **19** (R_F 0.25; 180 mg, 79%).

*1-Acetyl-3-(2,3-di-*O*-acetyl-5-*O*-p-nitrobenzoyl-β-*D*-ribofuranosyl)-6-nitroindole* (**22**). — Treatment of **18** (50 mg) in pyridine (3 ml) with acetic anhydride (2 ml) for 12 h at 20°, followed by concentration and p.l.c. of the residue (solvent *C*), gave **22** (R_F 0.43; 40 mg, 63%).

*3-(2,3-Di-*O*-acetyl-5-*O*-p-nitrobenzoyl-β-*D*-ribofuranosyl)-5-nitroindole* (**23**). — Similar acetylation of **19** (30 mg) gave, after p.l.c. (solvent *B*), **23** (R_F 0.50; 25 mg, 72%).

3-β-D-Ribofuranosyl-6-nitroindole (**20**). — A mixture of **18** (150 mg) and methanolic ammonia (5 ml) was kept at 20° for 12 h and then concentrated. The residue was purified by p.l.c. (solvent *C*), to give **20** (R_F 0.22; 80 mg, 80%).

3-β-D-Ribofuranosyl-5-nitroindole (**21**). — Similar treatment of **19** (310 mg) with methanolic ammonia (8 ml) gave **21** (R_F 0.33; 170 mg, 82%).

1-Acetyl-6-nitro-3-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)indole (**24**). — Acetylation of **20** (20 mg), as described for **18**, gave, after p.l.c. (solvent *B*), **24** (R_F 0.41; 20 mg, 64%). Mass spectrum: *m/z* 462 (M^+), 432 (M^+ — NO), 402, 342, 282 (M^+ — *n*·MeCOOH, *n* = 1, 2, or 3), 360, 300, 240 (M^+ — *n*·MeCOOH — C_2H_2O, *n* = 1, 2, or 3), and 190 (B + 30 — MeCO)$^+$.

5-Nitro-3-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)indole (**25**) *and 1-acetyl-5-nitro-3-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)indole* (**26**). — Treatment of **21** (60 mg) with pyridine (3 ml) and acetic anhydride (2 ml), as described for **18**, gave **25** (R_F 0.28; 40 mg, 49%) and **26** (R_F 0.33; 20 mg, 22%). Mass spectra **25**: *m/z* 420 (M^+), 360, 300, 240 (M^+ — *n*·MeCOOH, *n* = 1, 2, or 3), 204 (B + 43)$^+$, and 190 (B + 29)$^+$; **26**: *m/z* 462 (M^+), 402, 342, 282 (M^+ — *n*·MeCOOH, *n* = 1, 2, or 3), 360, 300, 240 (M^+ — *n*·MeCOOH — C_2H_2O, *n* = 1, 2, or 3), and 190 (B + 30 — $MeCO^+$).

1-Acetyl-3-(3-O-acetyl-5-O-p-nitrobenzoylpentosyl)-2-(or 3)-C,2'-O-isopropylidene-5-nitroindole (**34** or **35**). — A suspension of **17** (200 mg) in M methanolic hydrochloric acid (11 ml) was stirred at 20° for 12 h, and then neutralised with saturated aqueous $NaHCO_3$, and evaporated. A solution of the residue in acetone was filtered and concentrated, and p.l.c. then gave the compound (120 mg) with R_F 0.20 (solvent *B*). Treatment of this compound with pyridine (4 ml) and acetic anhydride (2 ml), as described for **18**, yielded **34** (**35**) (R_F 0.42; 100 mg, 42%).

1-(2-Deoxy-D-erythro-pentofuranosyl)-6-nitroindole (**39**). — A mixture of crude **37** (470 mg) and 0.1M methanolic sodium methoxide (15 ml) was stirred at 20° for 2 h. Dowex (H^+) resin was added to obtain a pH of 7.0, the filtered solution was evaporated, the residue was dissolved in methanol (1.5 ml), and p.l.c. (ethyl acetate–methanol, 10:1) then gave **39** (R_F 0.56, 100 mg).

P.m.r. data (CD_3OD) at 25°: δ 8.55 (d, H-7), 8.02 (dd, H-5), 7.87 (d, H-2), 7.63 (d, H-4), 6.65 (d, H-3), 6.47 (m, H-1'), 4.50 (H-3'), 4.07 (H-4'), 3.90–3.50 (H-5',5'), and 3.0–2.0 (H-2',2').

3-(2-Deoxy-D-erythro-pentofuranosyl)-6-nitroindole (**40**). — Similar treatment of **38** (300 mg) with 0.1M methanolic sodium methoxide (10 ml) yielded **40** (R_F 0.36; 20 mg, 71%).

P.m.r. data (CD_3OD) at 25°: δ 8.28 (d, H-7), 8.0–7.7 (m, H-4,5), 7.60 (s, H-2), 5.46 (m, H-1'), 4.42 (H-3'), 3.99 (H-4'), 3.90–3.50 (H-5',5'), 2.66 (H-2'a of one isomer), 2.24 (H-2'b of one isomer and H-2',2' of the other isomer).

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