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THE SYNTHESIS OF SOME 1-GLYCOSYL-6-NITROINDOLES

TATIANA D. MINIKER, VICTOR I. MUKHANOV, NIKOLAY D. CHKANIKOV, IRINA V. YARTZEVA, AND MARIA N. PREOBRAZHENSKAYA

Cancer Research Center of the USSR Academy of Medical Sciences, Moscow (U.S.S.R.)

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ABSTRACT

Condensation of 6-nitroindoline with 5-*O*-trityl-L-arabinose, -D-fucose, -D-arabinose, or -L-rhamnose gave the corresponding 1-glycosyl-6-nitroindolines, from which, after acetylation, dehydrogenation, and removal of protecting groups, 1-α- and -β-L-arabinofuranosyl, 1-β-D-fucopyranosyl, 1-α-D-arabinopyranosyl, and 1-α- and -β-L-rhamnopyranosyl derivatives of 6-nitroindole were obtained. The configuration of the arabinose and fucose derivatives was established by p.m.r. spectroscopy. Comparison of the p.m.r. and c.d. spectra of the products obtained from the glycosyl-nitroindoles by application in sequence of periodate oxidation, borohydride reduction, and acetylation allowed assignment of the configuration of the rhamnose derivatives.

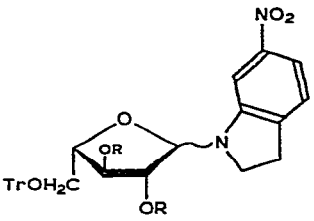
INTRODUCTION

Glycosylindoles are of interest as potential anticancer substances; 1-α-L-arabinopyranosyl derivatives of indole and some substituted indoles inhibit the growth of transplanted tumours in mice[1]. We now report the synthesis of some analogues of 1-α-L-arabinopyranosylindole.

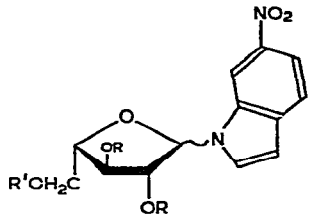
RESULTS AND DISCUSSION

Reaction of 5-*O*-trityl-L-arabinofuranose with 6-nitroindoline in boiling alcohol, in the presence of ammonium sulphate, gave 6-nitro-1-(5-*O*-trityl-L-arabinofuranosyl)-indoline (**1**) which, with acetic anhydride–pyridine, gave the diacetate **2**. Dehydrogenation of crude **2** with active manganese dioxide in boiling benzene gave 1-(2,3-di-*O*-acetyl-5-*O*-trityl-α-L-arabinofuranosyl)-6-nitroindole (**3**) and its β anomer (**4**) in the ratio 19:1. Treatment of **3** and **4** for 5 min with boiling 80% acetic acid effected detritylation and gave **5** and **6**. Deacetylation of **5** afforded 1-α-L-arabinofuranosyl-6-nitroindole (**7**; 54% overall yield). Some data on **3**–**5** and **7** are given in Tables I and II.

The p.m.r. data (Table II) confirm the α configuration for **3**, **5**, and **7**, and the β configuration for **4** and **6**. For the pairs **3**/**4** and **5**/**6**, the signal for the anomeric proton of the β anomer is downfield relative to that of the α anomer. These data agree with the finding[2,3] that the deshielding of the anomeric proton in nucleosides where



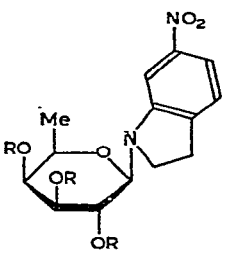
1 R = H
2 R = Ac



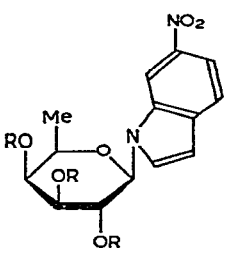
3 R = Ac, R′ = Tr ; α anomer
4 R = Ac, R′ = Tr ; β anomer
5 R = Ac, R′ = H ; α anomer
6 R = Ac, R′ = H ; β anomer
7 R = R′ = H ; α anomer

the aglycon and HO-2′ are *cis* is greater than that for the *trans* analogues. Due to the anisotropy of the indole moiety, the signals for AcO-2′ of the β compounds **4** and **6** are considerably up-field of the corresponding signals for the α anomers **3** and **5**. Likewise, H-4′ in **3** or **5** is deshielded in relation to H-4′ in **4** or **6**, because of the anisotropy of the aglycon, in a manner analogous to that for D-ribosyl derivatives of 5- and 6-fluoroindole[2].

Using the above reactions, D-fucose was converted into 1-β-D-fucopyranosyl-6-nitroindoline (**8**) and the triacetate (**9**), and thence, *via* **10**, into 1-β-D-fucopyranosyl-6-nitroindole (**11**).



8 R = H
9 R = Ac



10 R = Ac
11 R = H

Analytical and p.m.r. data for **8–11** are given in Tables I and III, respectively. The magnitude (9 Hz) of $J_{1',2'}$, for **8–11** indicates that H-1 and H-2 are *trans*-diaxial, that the configuration is β, and that the conformation is $^4C_1$. The signal for AcO-2′ is shifted upfield by 0.25 p.p.m. in going from the indoline **9** to the indole **10**, because of the anisotropy of the indole ring. This difference confirms the *trans*-diequatorial relationship of the indole ring and AcO-2′, and reflects the preferred anti-conformation at the C-1′–N bond[4].

The α-D-arabinopyranosyl derivatives **12–15** were obtained from D-arabinose and 6-nitroindoline by using the reactions previously noted; analytical and p.m.r. data are given in Tables I and II, respectively. The magnitude (9–10 Hz) of $J_{1',2'}$ and $J_{2',3'}$ indicates the axial orientation of H-1′,2′,3′, the α configuration, and the $^1C_4$ conformation.

TABLE I

DATA FOR SOME 1-GLYCOSYL-6-NITROINDOLES

Compound	*Yield* (%)	λ_{max}^{EtOH} (*log ε*)	$[\alpha]_D^{20}$ (*methanol*) (*degrees*)	*Found* (%)	*Calc.* (%)	*Formula*
3	70.0	212(4.56) 234(4.12)(sh)[a] 250(3.95) 315(3.86) 357(3.78)	−62.0 (*c* 0.82)[b]	67.6 5.0 4.8	67.8 5.3 4.5	$C_{36}H_{32}N_2O_8 \cdot H_2O$
4	3.6	211(4.56) 234(4.08)(sh) 250(3.86) 315(3.72) 357(3.60)	+56.0 (*c* 0.5)[b]	67.9 5.3 4.4	67.8 5.3 4.5	$C_{36}H_{32}N_2O_8 \cdot H_2O$
5	85.5	211(4.19) 250(3.81) 315(3.75) 357(3.64)		52.7 4.9 8.0	52.4 5.1 7.2	$C_{17}H_{18}N_2O_8 \cdot 0.25H_2O$
7	90.0	212(4.12) 249(3.72) 318(3.64) 358(3.55)	−42.3 (*c* 1.0)[c]	53.4 4.9 9.8	53.1 4.8 9.6	$C_{13}H_{14}N_2O_6$
8	72.2	255(4.15)	−84.4 (*c* 1.0)	54.0 6.5 9.1	54.2 5.9 9.1	$C_{14}H_{18}N_2O_6$
9	68.4	252(4.19)	+1.4 (*c* 1.0)	54.8 5.6	55.1 5.5	$C_{20}H_{24}N_2O_9$
10	55.1	212(4.22) 247(3.97) 318(3.91) 352(3.85)	−108.2 (*c* 1.0)	55.5 5.2 6.8	55.3 5.1 6.4	$C_{20}H_{22}N_2O_9$
11	90.0	212(4.28) 246(3.95) 318(3.88) 357(3.82)	+3.5 (*c* 1.0)	53.5 5.4 9.1	53.8 5.3 9.0	$C_{14}H_{16}N_2O_6 \cdot 0.25H_2O$
12	76.0	252(4.12)	−65.8 (*c* 1.8)			

TABLE I (continued)

Compound	*Yield* (%)	λ_{max}^{EtOH} (*log* ε)	$[\alpha]_D^{20}$ *(methanol) (degrees)*	*Found* (%)	*Calc.* (%)	*Formula*
13	83.5	252(4.11)	−43.7 (*c* 1.0)	54.0 5.3 6.6	54.0 5.3 6.6	$C_{19}H_{22}N_2O_9$
14	76.8	212(4.27) 247(3.95) 318(3.89) 356(3.80)	+117.2 (*c* 1.0)	54.0 4.9	54.3 4.8	$C_{19}H_{20}N_2O_9$
15	100.0	212(4.29) 249(3.98) 320(3.92) 357(3.86)	−48.2 (*c* 1.0)	53.2 4.9 9.2	53.1 4.8 9.5	$C_{13}H_{14}N_2O_6$
16	33.0	210(4.38) 248(3.97) 320(3.88) 357(3.83)	−44.5 (*c* 0.86)[b]	55.4 5.2 6.5	55.3 5.1 6.4	$C_{20}H_{22}N_2O_9$
18	90.0	211(4.36) 248(4.01) 318(3.90) 359(3.81)	−1.6 (*c* 0.86)	51.4 5.6 8.8	51.5 5.6 8.6	$C_{14}H_{16}N_2O_6 \cdot H_2O$

[a]sh, shoulder. [b]In chloroform. [c]In acetone.

TABLE II

P.M.R. DATA[a] FOR THE CARBOHYDRATE MOIETY OF 1-L- AND -D-ARABINOSYL-6-NITROINDOLES

Compound	*Chemical shifts (δ, p.p.m.)*							*Coupling constants (Hz)*						*Solvent,*
	H-1′	*H-2′*	*H-3′*	*H-4′*	*H-5′a*	*H-5′b*	*O-Ac*	$J_{1',2'}$	$J_{2',3'}$	$J_{3',4'}$	$J_{4',5'a}$	$J_{4',5'b}$	$J_{5'a,5'b}$	*temperature*
3	6.25d	6.01–5.45m		4.49m		3.48m	2.07s 2.03s	3.5		3.0				$CDCl_3$, 20°
4	6.81d	5.50q	5.25q	4.21m		3.54m	2.10s 1.57s	5.0	3.0	4.5				Me_2SO-d_6, 70°
5	6.29d	5.71t	5.45q	4.41m		3.95m	2.13s (2 groups)	3.5	3.0	4.2				$CDCl_3$, 22°
6	6.50d	5.58–5.41m		4.18–3.92m			2.17s 1.64s	5.0						$CDCl_3$, 22°
7	6.04d	4.37m		4.11m		3.65m	—	3.4						Me_2SO-d_6, 25°
12	4.68d	4.05–3.40m					—	9.0						CD_3OD, 20°
13	4.89d	5.52q	5.16dd	5.34m	4.05dd	3.92– 3.64m[b]	2.19s 2.03s 2.00s	9.1	10.0	3.5	2.0		14.0	$CDCl_3$, 20°
14	5.43d	5.74q	5.23dd	5.43m	4.22dd	3.89dd	2.36s 2.00s 1.68s	9.0	10.0	3.5	2.3	1.0	13.0	$CDCl_3$, 20°
15	5.48d	4.20–3.20m					—	9.0						CD_3OD, 20°

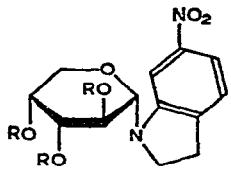
[a]Signal multiplicities: d, doublet; m, multiplet; q, quartet, t, triplet. [b]The signal overlaps those of the indoline moiety.

TABLE III

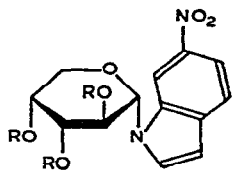
P.M.R. DATA[a] FOR THE CARBOHYDRATE MOIETY OF SOME 1-D-FUCOPYRANOSYL- AND 1-L-RHAMNOPYRANOSYL DERIVATIVES OF 6-NITROINDOLE

Compound	*Chemical shifts (δ, p.p.m.)*							*Coupling constants (Hz)*					*Solvent, temperature*
	H-1'	*H-2'*	*H-3'*	*H-4'*	*H-5'*	*CMe*	*O-Ac*	$J_{1',2'}$	$J_{2',3'}$	$J_{3',4'}$	$J_{4',5'}$	$J_{5',Me}$	
8	4.74d	3.21–4.05m[b]				1.19d	—	9.0				6.3	CD_3OD, 50°
9	4.94d	5.51t	5.17dd	5.30dd	4.12–3.56m[b]	1.16d	2.21s 2.00s 1.97s	9.0		3.5	1.5	6.5	$CDCl_3$, 20°
10	5.61d	5.77t	5.28dd	5.44dd	4.15q	1.32d	2.37s 2.00s 1.72s	9.0	9.0	3.5	1.0	6.3	$CDCl_3$, 20°
11	5.40d	4.14t	4.04–3.48m			1.28d	—	9.0				6.5	CD_3OD, 20°
16	5.94d	5.56m	5.20–5.40m		3.86q	1.32d	2.03s 1.95s 1.92s	1.5	2.3		9.4	6.0	$CDCl_3$, 20°
16[c]	5.96d	5.58m	5.30dd	5.23t	3.85q	1.36d	2.06s 2.02s 1.99s	1.5	2.1	9.5	9.5	6.1	$CDCl_3$, 20°
17		5.97s	5.62–5.11m		3.68m	1.33d	2.12s 2.09s 2.08s			8.5	7.5	6.5	$CDCl_3$ + Me_2SO-d_6, 20°
	[d]	6.05t	5.48–5.20m[d]		3.31m	1.08d	1.78s 1.71s 1.65s	>2	>2			6.6	C_6D_6, 20°
18	6.04d	4.16–3.15m				1.29d	—	1					Me_2SO-d_6, 25°
19	5.90d	4.43q	3.92q	3.80–3.16m		1.31d	—	5.4	3.6			6.2	CD_3OD + Me_2SO-d_6, 50°

[a]Signal multiplicities: d, doublet; m, multiplet; q, quartet; s, singlet; t, triplet. [b]The signals overlap those of the indoline moiety. [c]The spectrum was recorded with a Bruker WH 360-MHz instrument. [d]Overlapping signals.



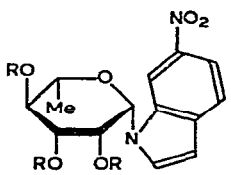
12 R = H
13 R = Ac



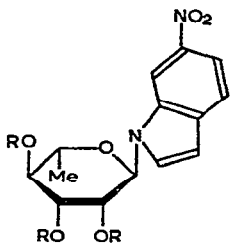
14 R = Ac
15 R = H

Comparison of the p.m.r. data for the indoline and indole derivatives **13** and **14** reveals the anisotropic effect of the indole nucleus on the chemical shift of AcO-2′ in **14**.

Application of the above reactions to L-rhamnose gave, first, a mixture of 6-nitro-1-β-L-rhamnopyranosylindoline and its α anomer, as indicated by the double p.m.r. signals for Me-5′. The mixture was acetylated and the products were dehydrogenated to give a mixture of anomers (**16**/**17**) from which crystalline 6-nitro-1-(2,3,4-tri-*O*-acetyl-β-L-rhamnopyranosyl)indole (**16**) was then isolated and deacetylated to give 6-nitro-1-β-L-rhamnopyranosylindole (**18**). Deacetylation of the residual anomeric mixture (**16**/**17**) and repeated t.l.c. of the product gave the α anomer **19**, from which the triacetate **17** was obtained. The analytical data for **16** and **18** are given in Table I, and the p.m.r. data for **16**–**19** in Table III.



16 R = Ac
18 R = H



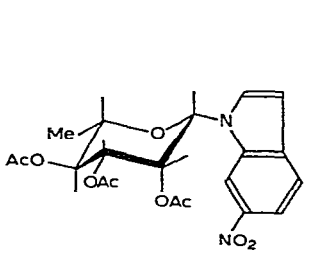
17 R = Ac
19 R = H

The p.m.r. data for **16** and **17** do not allow unequivocal determination of the stereochemistry. From the values (9.5 Hz) of $J_{3',4'}$ and $J_{4',5'}$ for the β anomer **16**, a $^1C_4$ conformation may be inferred; $J_{1',2'}$ for **16** is 1.5 Hz.

The p.m.r. spectrum for the α anomer **17** in $CDCl_3$ contains a broad, two-proton singlet at δ 5.97 for H-1′,2′. In C_6D_6, the signal for H-2′ is a broad triplet at δ 6.05 (signal width, 5.6 Hz), and that for H-1′ is shifted up-field and merges with the signals for H-3′ and H-4′, forming an unsymmetrical, three-proton multiplet at δ 5.28–5.60. Thus, it may be concluded that $J_{1',2'}$ for **17** is > 2 Hz.

Magnin *et al.*[5] have shown that the carbohydrate moiety in acetylated L-rhamnopyranosyl derivatives of indole and 5-nitroindole is in the $^1C_4$ conformation; for a pair of anomers, they suggested that the anomer having the larger $J_{1',2'}$ value has H-1′ axial and H-2′ equatorial, *i.e.*, it is the β anomer. However, for α- and β-L-rhamnopyranose and the methyl glycosides in the $^1C_4$ conformation, it has recently

been shown[6] that the α compounds have the higher value of $J_{1',2'}$. In the reactions described herein, we presume that the preponderant formation of the β anomer **16** is due to the preference of the bulky 6-nitroindole residue for the equatorial position (**20**). This view is supported by the conformational instability of the α anomer **17** which, in solution, exists as an equilibrium of $^1C_4$ and $^4C_1$ conformers (**21**⇌**22**).



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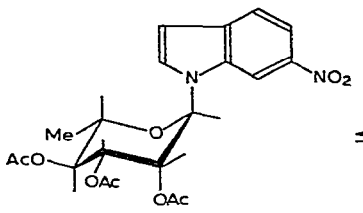

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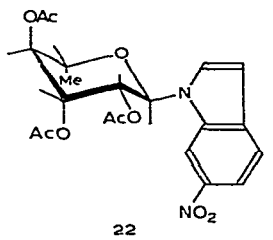

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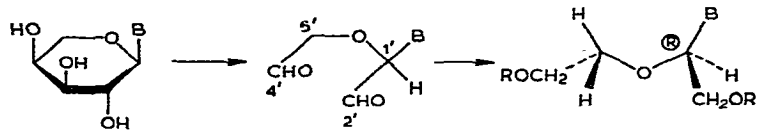
Since the structure of the rhamnopyranosyl derivatives **18** and **19** could not be rigorously established by the p.m.r. method, the products of periodate oxidation were studied. Periodate oxidation of 1-glycosylindoles results in almost concurrent attack of the carbohydrate and indole moieties. However, the presence of a nitro group stabilises the aglycon and selective oxidation of the carbohydrate portion is possible[7]. Oxidation of 1-α-L-arabinopyranosyl (**23**), 1-α-L-arabinofuranosyl (**7**), 1-β-D-fucopyranosyl (**11**), 1-β-L-rhamnopyranosyl (**18**), and 1-α-L-rhamnopyranosyl (**19**) derivatives of 6-nitroindole with periodic acid at room temperature gave the corresponding "dialdehydes" **24–28**, which showed no i.r. absorption for carbonyl and had p.m.r. spectra indicative of complex mixtures of hydrated, cyclic acetal forms.

TABLE IV

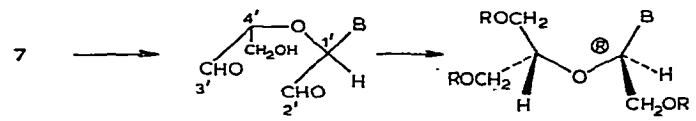
PROPERTIES OF COMPOUNDS **29–32** AND **34–38**

Compound	*Yield* (%)	R_F *(Silica gel)*	*U.v.:* λ_{max}^{EtOH}, *nm (log ε)*	*C.d.:* λ_{max}^{EtOH}, *nm (θ)*
29	65[a]	0.39[d]	250(3.89), 319(3.79), 352(3.68)	305 (+1800)
30	66[a]	0.34[d]	250(3.93), 321(3.85), 365(3.76)	305 (+1800)
31	64[a]	0.50[d]	252(3.98), 313(3.82), 360(3.76)	305 (+1650)
32	66[b]	0.50[d]	250(3.96), 320(3.88), 365(3.68)	305 (−1650)
34	65[c]	0.62[e]	247(3.95), 316(3.83), 358(3.72)	310 (+1550)
35	70[c]	0.49[e]	240(3.60), 316(3.83), 360(3.40)	305 (+1500)
36	66[c]	0.57[e]	247(3.98), 315(3.86), 360(3.75)	305 (+2800)
37	59[c]	0.47[f]	247(3.98), 315(3.87), 360(3.73)	305 (−2800)
38	6[c]	0.37[f]	250(3.96), 320(3.88), 355(3.79)	310 (+650) 267 (−950)

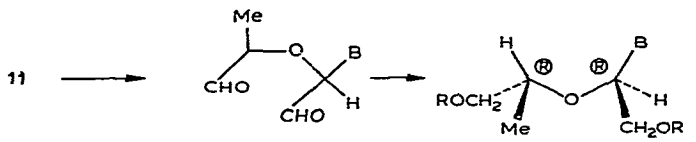
[a]Calculated on appropriate 1-glycosyl-6-nitroindole. [b]Calculated on diacetate **37**. [c]Calculated on appropriate diol (or triol). [d]Solvent system: benzene–acetone (1 : 1). [e]Solvent system: benzene–acetone (4 : 1). [f]Solvent system: carbon tetrachloride–acetone (10 : 1).



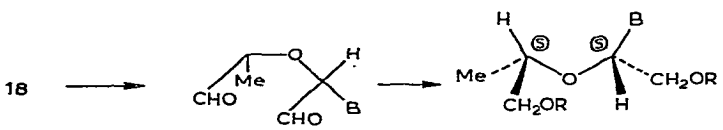
23 24 29 R = H
34 R = Ac



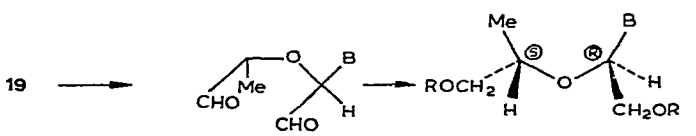
25 30 R = H
35 R = Ac



26 31 R = H
36 R = Ac



27 32 R = H
37 R = Ac



28 33 R = H
38 R = Ac

Dialdehydes **24–26** were severally reduced with sodium borohydride to give the corresponding diols and triol **29–31**; the diol **32** was obtained indirectly. Data on **29–32** are given in Table IV; all the compounds have u.v. absorption maxima characteristic of 6-nitroindole derivatives, indicating that the nitroindole moiety had not been affected. The p.m.r. spectra of the alcohols **29–32** contained signals for the protons of the substituted indole nucleus, and also triplets for H-1′ at $\delta \sim 6$, consistent with a -CH-CH_2 grouping.

Spectral data on the acetates (**34–38**) of the alcohols **29–33** are given in Tables IV and V. The mixture of acetates **37** and **38**, obtained by periodate oxidation of a

TABLE V

P.M.R. DATA[a,b] FOR DERIVATIVES **29–32** AND **34–38**

Compound	*Chemical shifts (δ, p.p.m.)*											*Solvent, temperature*
	H-7	*H-5*	*H-4*	*H-3*	*H-2*	*H-1'*	*H-2'*	*H-4'(3')*	*H-5'(4')*	*C-Me*	*O-Ac*	
29	8.67d	8.01dd	7.68d	6.68d	7.74d	5.80t	3.21m	3.71–3.35m		—	—	CD_3OD, 20°
30	8.64d	7.96dd	7.66d	6.68d	7.78d	6.07t		4.20–3.68m		—	—	CD_3OD, 20°
31	8.60d	7.98dd	7.66d	6.68d	7.72d	5.98t		4.18–3.44m		0.86d	—	CD_3OD, 20°
32	8.64d	7.98dd	7.66d	6.68d	7.72d	5.98t		4.18–3.44m		0.88d	—	CD_3OD, 20°
34	8.39d	7.93dd	7.54d	6.61d	7.41d	5.76t	4.43m	4.15m	3.60m	—	1.97s 1.89s	$CDCl_3$, 20°
35	8.47d	8.06dd	7.67d	6.68d	7.50d	6.06t		4.63–3.74m		—	2.14s 1.90s 1.73s	$CDCl_3$, 20°
36	8.62d	8.14dd	7.76d	6.78d	7.62d	6.18t	4.73–4.00m		3.80m	1.02d	2.16s 1.90s	$CDCl_3$, 20°
37	8.52d	8.09dd	7.72d	6.71d	7.53d	6.07t	4.43m	4.13m	3.76m	1.02d	2.15s 1.92s	$CDCl_3$, 25°
38	8.48d	8.09dd[c]	7.65d	6.65d	7.51d	5.86t	4.42m	3.90m	3.73m	1.28d	1.90s 1.74s	$CDCl_3$, 20°

[a]Signal multiplicities: d, doublet; m, multiplet; s, singlet; t, triplet. [b]Coupling constants: $J_{5,7}$ 2; $J_{4,5}$ 8; $J_{2,3}$ 3; $J_{Me,5'}$ 6; $J_{1',2'}$ 6. Hz. [c]Coupling constant: $J_{4,5}$ 9 Hz.

TABLE VI

MASS SPECTRA OF ACETATES **34–38**

Compound	m/e	*Relative intensity* (%)	*Fragment*
34	350	6	M^+
	189	15	$(AcO\text{-}CH_2\text{-}CH_2\text{-}O\text{-}CH\text{-}CH_2OAc)^+$
	87	100	$(CH_2\text{-}CH_2\text{-}OAc)^+$
	247	3	$(B\text{-}CH\text{-}CH_2\text{-}OAc)^+$
	43	75	$(Ac)^+$
35	420	9	M^+
	261	13	$(AcO\text{-}CH_2\text{-}CH(CH_2\text{-}OAc)\text{-}O\text{-}CH\text{-}CH_3\text{-}OAc)^+$
	159	65	$(AcO\text{-}CH_2\text{-}CH\text{-}CH_2\text{-}OAc)^+$
	247	9	$(B\text{-}CH\text{-}CH_2\text{-}OAc)^+$
	43	100	$(Ac)^+$
36	364	10	M^+
	203	10	$(AcO\text{-}CH_2\text{-}CH(Me)\text{-}O\text{-}CH\text{-}CH_2\text{-}OAc)^+$
	101	63	$(AcO\text{-}CH_2\text{-}CH(Me))^+$
	247	15	$(B\text{-}CH\text{-}CH_2\text{-}OAc)^+$
	43	100	$(Ac)^+$
37	364	21	M^+
	203	21	$(AcO\text{-}CH_2\text{-}CH(Me)\text{-}O\text{-}CH\text{-}CH_2\text{-}OAc)^+$
	101	74	$(AcO\text{-}CH_2\text{-}CH(Me))^+$
	247	21	$(B\text{-}CH\text{-}CH_2\text{-}OAc)^+$
	43	100	$(Ac)^+$
38	364	4	M^+
	203	9	$(AcO\text{-}CH_2\text{-}CH(Me)\text{-}O\text{-}CH\text{-}CH_2\text{-}OAc)^+$
	101	39	$(AcO\text{-}CH_2\text{-}CH\text{-}Me)^+$
	247	4	$(B\text{-}CH\text{-}CH_2\text{-}OAc)^+$
	43	100	$(Ac)^+$

mixture of the α- and β-rhamnosyl derivatives **18** and **19** followed by reduction and acetylation, was fractionated by t.l.c., and the pure ester **37** was saponified to give the alcohol **32**. According to the p.m.r. data, the ratio of **18** and **19** in the initial mixture was ~6:1.

Mass-spectral data for the acetates **34–38** are given in Table VI. Peaks for molecular ions (M^+) were observed, and decomposition of the molecular ions

paralleled that for the molecular ions of ethers[6]. Loss of the indole radical (B) from the most-branched α-carbon atom of the ether occurs, and other fragments are formed by cleavage of the ether C–O bonds (Table VI).

In compounds **29**, **30**, **34**, **35** (from α-L-arabinosyl derivatives), **33**, **38** (from the α-L-rhamnosyl derivative), **31**, and **36** (from the β-D-fucosyl derivative), the glycosyl centre (C-1′) has the *R* configuration; in compounds **32** and **37** (from the β-L-rhamnosyl derivative), it has the *S* configuration. In **29**, **30**, **34**, and **35**, there is no second chiral centre; in the L-rhamnosyl derivatives **32**, **33**, **37**, and **38**, the second chiral centre has the *S* configuration; and in **31** and **36**, it has the *R* configuration. Thus, the derivatives (**31**,**36**) obtained from the β-D-fucosylindole are enantiomers of the derivatives (**32**,**37**) obtained from the β-L-rhamnopyranosylindole, and diastereoisomers of the derivatives (**33**,**38**) obtained from the α-L-rhamnopyranosylindole.

The p.m.r. spectra (Table V) of the enantiomeric diols **31** and **32** and the diacetates **36** and **37** are very closely similar, whereas those for the diastereoisomeric diacetates **36** and **38** are significantly different. Thus, the structures assigned to the derivatives **18** and **19** are confirmed.

Further confirmation of the structures of the 6-nitroindole derivatives was furnished by the c.d. data in Table IV. Compounds **29**–**31** and **34**–**36**, which have the *R* configuration at the chiral centre associated with the chromophore group, display positive Cotton effects. Derivative **38** (from the α-L-rhamnosylindole) has a positive Cotton effect, whereas **32** and **37** (from the β-L-rhamnosylindole) have negative Cotton effects. The c.d. curves for the enantiomers **31** and **32** or **36** and **37** are symmetrical to the X-axis. Thus, the *S* configuration can be assigned to C-1′ in **32** and **37**, in agreement with the p.m.r. data. Unfortunately, the data available are not sufficiently accurate to allow quantitative comparison of Cotton effects for **29**–**32** and **34**–**38**. The corresponding derivatives **29**/**30** and **34**/**35** having only one chiral centre (C-1′) show similar Cotton effects. Comparison of the c.d. data for **29**–**32** shows that the introduction of a second chiral centre (C-5′) causes no change in the Cotton effect. Coincidence of the configurations of the chiral centres at C-5′ and C-1′ increases the amplitude of the Cotton effect, as shown by comparing the data for the acetates **36** and **37** with those for **34** and **35**. Different chirality at C-1′ and C-5′, as in the acetate **38**, decreases the amplitude of the Cotton effect as compared with acetates **34** and **35**.

EXPERIMENTAL

General. — P.m.r. spectra were recorded with a JEOL JNM-MH-100 instrument, u.v. spectra with a Unicam SP-800 spectrophotometer, c.d. spectra with a Roussel–Jouan II Dichrograph, and mass spectra with an LKB-9000 instrument operating at 70 eV with an ion-source temperature of 80–90° and the direct-insertion procedure. Optical rotations were determined with a Perkin–Elmer 241 polarimeter. Silufol UV-254 and silica gel LCL_{254} 5/40 were used for t.l.c. Unless otherwise specified, R_F values refer to Silufol. The yields and properties of the 6-nitroindole derivatives are given in Tables I and IV.

1-(2,3-Di-O-acetyl-5-O-trityl-α- and -β-L-arabinofuranosyl)-6-nitroindole (**3** *and* **4**). — A mixture of 5-*O*-trityl-L-arabinose[9] (1.55 g) and 6-nitroindoline[10] (0.8 g) in ethanol (150 ml) was boiled for 12 h. The alcohol was evaporated, and acetic anhydride (8 ml) was added to a solution of the residue in dry pyridine (25 ml) at 0°. After storage overnight at 20°, the mixture was poured into ice–water (1 L), and the precipitate (**2**) was collected, dried *in vacuo*, and stirred with manganese dioxide[11] (12 g) in benzene for 4 h with azeotropic distillation of water. The cooled mixture was filtered and concentrated, and the residue was subjected to t.l.c. (silica gel; benzene–acetone, 20:1, 4 developments) to give **3** (1.72 g), R_F 0.36, and **4** (0.09 g), R_F 0.32.

1-(2,3-Di-O-acetyl-α- and -β-L-arabinofuranosyl)-6-nitroindole (**5** *and* **6**). — A mixture of **3** (1.72 g) and 80% acetic acid (17 ml) was boiled for 5 min, then cooled, filtered, and concentrated *in vacuo*. The oily residue was subjected to t.l.c. (silica gel; chloroform–ethyl acetate, 3:2). The zone with R_F 0.19 was eluted to give **5** (0.9 g) as an oil.

In a similar manner, **4** (0.09 g) was converted into **6** (0.04 g, 72.9%), R_F 0.22.

1-α-L-Arabinofuranosyl-6-nitroindole (**7**). — To a solution of **5** (1.25 g) in methanol (15 ml) was added methanolic 0.1M sodium methoxide (3 ml). The mixture was stirred at 20° for 15 min, neutralized with Dowex-50(H^+) resin, filtered, and concentrated. The residue was triturated with water to give **7** (0.88 g) as a solid foam, R_F 0.31 (benzene–acetone, 1:1).

1-β-D-Fucopyranosyl-6-nitroindoline (**8**). — A mixture of D-fucose (5.26 g), 6-nitroindoline (5.8 g), and ammonium sulphate (1.4 g) in ethanol (700 ml) was boiled for 12 h, cooled, stirred with active carbon (1 g) for 10 min, filtered, and concentrated *in vacuo*. The residue was triturated with chloroform to give **8** (7.23 g) as a solid foam, R_F 0.27 (benzene–acetone, 2:3).

6-Nitro-1-(2,3,4-tri-O-acetyl-β-D-fucopyranosyl)indoline (**9**). — To a solution of **8** (6.73 g) in dry pyridine (150 ml) was added acetic anhydride (70 ml) at 0°. The mixture was stored overnight at 20° and then poured into ice–water (5 L). The precipitate (6.47 g) was collected, dried *in vacuo*, and recrystallised from ethanol to give **9**, m.p. 135–137°, R_F 0.42 (benzene–acetone, 10:1).

6-Nitro-1-(2,3,4-tri-O-acetyl-β-D-fucopyranosyl)indole (**10**). — A solution of **9** (5.47 g) in dry benzene (250 ml) was boiled and stirred with MnO_2 (28 g), with azeotropic distillation of water, for 7 h, and then cooled, filtered, and concentrated. The residue was crystallised from ethanol to give **10** (3 g), m.p. 146–147°, R_F 0.32 (benzene–acetone, 10:1).

1-β-D-Fucopyranosyl-6-nitroindole (**11**). — Deacetylation of **10** (2.5 g), as described for **7**, gave **11** (1.62 g), m.p. 105–107°, R_F 0.43 (benzene–acetone, 2:3).

1-α-D-Arabinopyranosyl-6-nitroindoline (**12**). — Reaction of D-arabinose (30 g) with 6-nitroindoline (3.5 g), as described for D-fucose, gave **12** as a solid foam, R_F 0.5 (benzene–acetone, 2:3).

6-Nitro-1-(2,3,4-tri-O-acetyl-α-D-arabinopyranosyl)indoline (**13**). — Acetylation

of **12** (4.2 g), as described for **8**, gave **13** (5 g), m.p. 78–80° (from ethanol), R_F 0.32 (carbon tetrachloride–acetone, 4:1).

*6-Nitro-1-(2,3,4-tri-*O*-acetyl-α-*D*-arabinopyranosyl)indole* (**14**). — Treatment of **13** (4.5 g) with MnO_2, as described for **10**, gave **14** (3.44 g), m.p. 157–157.5° (from ethanol), R_F 0.23 (carbon tetrachloride–acetone, 4:1).

*1-α-*D*-Arabinopyranosyl-6-nitroindole* (**15**). — Deacetylation of **14** (2.2 g), as described for **7**, gave **15** (1.5 g), m.p. 192–193° (from methanol), R_F 0.23 (benzene–acetone, 2:3).

*6-Nitro-1-(2,3,4-tri-*O*-acetyl-αβ-*L*-rhamnopyranosyl)indole* (**17,16**). — A mixture of L-rhamnose (3 g), 6-nitroindoline (3 g), $(NH_4)_2SO_4$ (0.75 g), and ethanol (100 ml) was boiled for 12 h, cooled, stirred with active carbon (0.5 g) for 10 min, filtered, and concentrated *in vacuo*. The residue was crystallized from methanol to give 6-nitro-1-αβ-L-rhamnopyranosylindoline (4.07 g), a portion (3 g) of which was conventionally treated with pyridine (70 ml) and acetic anhydride (30 ml) to give an anomeric mixture of triacetates (3.46 g). A portion (2.9 g) was treated with MnO_2 (12 g), as described for **9**, to give a mixture of **16** and **17** in the ratio 5:1 (p.m.r. spectroscopy) as a solid foam. Crystallisation of the mixture from ethanol (30 ml) gave the β anomer **16** (2.43 g), R_F 0.45 (carbon tetrachloride–ethyl acetate, 4:1).

*6-Nitro-1-β-*L*-rhamnopyranosylindole* (**18**). — Deacetylation of **16** (1 g), as described for **7**, gave **18** (0.63 g), R_F 0.36 (ethyl acetate).

*6-Nitro-1-α-*L*-rhamnopyranosylindole* (**19**). — The mother liquor from the crystallisation of **16** was concentrated and the residue (0.5 g) containing **16** and **17** was deacetylated, as described for **7**. 6-Nitroindole was extracted from the product with chloroform, and the residue (0.28 g) was subjected to t.l.c. (silica gel, ethyl acetate, 4 developments) to give **18** (0.02 g), a mixture of **18** + **19** (0.07 g), and **19** (0.07 g), R_F 0.29 (ethyl acetate).

Treatment of **19** (0.04 g) with acetic anhydride and pyridine, as described for **8**, gave the triacetate **17** (0.05 g, 94%) as an oil, $[\alpha]_D^{20}$ −128° (*c* 1, chloroform), R_F 0.45 (carbon tetrachloride–acetone, 4:1). Mass spectrum: *m/e* 434 (5%), 273 (18), 81 (48), and 43 (100).

Periodate oxidation of 1-glycosyl-6-nitroindoles and reduction of the resulting dialdehydes. — (*a*) To a solution of the 1-glycosyl-6-nitroindole (**7**, **11**, or **23**; 0.5 g) in methanol (20–100 ml) was added a solution of periodic acid (0.98 g; 0.49 g for **7**) in water (20 ml). The mixture was stored overnight at room temperature and then extracted with chloroform. The extract was washed twice with water, dried (Na_2SO_4), filtered, and concentrated, and the residue was dried *in vacuo*.

The dialdehydes (**24–26**) were obtained as yellow, amorphous substances. A solution of each in ethanol (40 ml) was stirred with $NaBH_4$ (0.2 g) for 0.5 h at 20°. Each mixture was treated with Amberlite *CG*-120(H^+) resin to pH 6, filtered, and concentrated, and methanol (5 × 6 ml) was distilled from the residue. Each residue was eluted from silica gel with acetone to give the alcohol (**29–31**) as a yellow oil. Each alcohol was treated with acetic anhydride (5 ml) and pyridine (10 ml), as

described for **8**, and the crude product was eluted from silica gel with acetone to give the acetate (**34–36**) as a yellow oil.

(*b*) 6-Nitro-1-$\alpha\beta$-L-rhamnopyranosylindole (0.34 g; **18**:**19**, 6:1), described above, was oxidised and reduced, as described in (*a*), to give a mixture of diols **32** and **33** (0.2 g, 65%) in the ratio 5:1 as indicated by p.m.r. spectroscopy. The mixture was acetylated, as described for **8**, to give a yellow oil (0.17 g) which was subjected to t.l.c. (silica gel; chloroform, 4 developments). Fractions with R_F 0.47 and 0.37 were extracted with acetone to give the diacetates **37** (0.155 g) and **38** (0.015 g), respectively, as yellow oils.

The diacetate **37** (0.06 g) was deacetylated as described for **7**, the product was subjected to t.l.c. (acetone), and the fraction with R_F 0.5 was extracted with acetone to give diol **32** (0.03 g, 66%) as a yellow oil.

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