Tetrahedron. Vol. 28, pp. 4099 to 4112. Pergamon Press 1972. Printed in Great Britain

HETEROCYCLIC N-GLYCOSYL DERIVATIVES—XIII
REACTION OF 6-CHLOROPURINE AND BENZOTRIAZOLES WITH ACETYLATED GLYCALS

M. FUERTES, G. GARCÍA-MUÑOZ, F. G. DE LAS HERAS, R. MADROÑERO and M. STUD
Instituto de Química Orgánica General, Departamento de Química Médica,
Juan de la Cierva, 3, Madrid-6, Spain

and

M. RICO

Instituto de Química-Física "Rocasolano", Serrano, 119, Madrid-6, Spain

(*Received in the UK* 14 *March* 1972; *Accepted for publication* 27 *April* 1972)

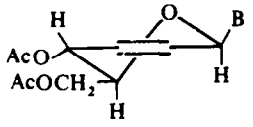
Abstract— Acid-catalysed reactions of tri-O-acetyl-D-glucal with benzotriazole, 5,6-dimethylbenzotriazole, 5,6-dichlorobenzotriazole and 6-chloropurine have been found to give anomeric mixtures of the corresponding 2′,3′-unsaturated N-glycosyl derivatives with the α-anomers preponderating. When tri-O-acetyl-D-galactal was used the 3′,4′,6′-tri-O-acetyl-α- and β-D-*lyxo*-hexopyranosyl nucleoside analogs were obtained. The conformation and anomeric configuration of all the N-glycosyl compounds obtained were assigned by NMR studies.

SINCE the initial suggestion of Robins *et al.*[1] of employing glycals in nucleoside synthesis, a variety of heterocyclic compounds have been shown to react with acylated glycals in the presence of acid catalyst (sulfanilic, trifluoracetic and *p*-toluenesulphonic acids).[2] The results have shown that either 2′,3′-unsaturated or 2-deoxypyranosyl nucleoside derivatives are formed depending on the *trans* or *cis* orientation of the vicinal acyloxy groups at C-3 and C-4 of the glycal used, respectively.

In continuing our work on the synthesis and transformation of purine nucleoside analogs we have now studied the acid-catalysed reactions of two hexopyranoid glycals, namely 3,4,6-tri-O-acetyl-D-glucal and 3,4,6-tri-O-acetyl-D-galactal, with benzotriazole, 5,6-dimethylbenzotriazole, 5,6-dichlorobenzotriazole and 6-chloropurine.

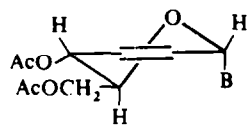
Condensation of tri-O-acetyl-D-glucal with the above benzotriazoles and 6-chloropurine afforded the corresponding 4,6-di-O-acetyl-2,3-dideoxy-D-*erythro*-hex-2-enopyranosyl derivatives (Ia–f and IIa–g, Fig 1) as anomeric mixtures in which the α-anomers invariably were the major constituents. However, the reaction of this glycal with 5,6-dimethylbenzotriazole and 6-chloropurine provided, in addition to the before mentioned unsaturated N-glycosyl compounds, the 2-deoxypyranosyl derivatives IIIb, d (β-anomers) and IVb, d (α-anomers). It is noteworthy that these products are unstable. Thus, the 5,6-dimethylbenzotriazole derivatives IIIb and IVb were both easily transformed by moderate heating or standing in solution at room temperature into 1-(4,6-di-O-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl)-5,6-dimethylbenzotriazole (IIb).

Structural, configurational and conformational assignments of all the products obtained (Fig 1) are based on analytical and spectroscopic data. Thus, the position of



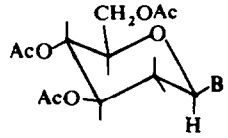
I

Ia B = Benzotriazol-1-yl
Ib B = 5,6-Dimethylbenzotriazol-1-yl
Ic B = 5,6-Dichlorobenzotriazol-1-yl
Id B = 6-Chloropurin-9-yl
Ie B = 5,6-Dimethylbenzotriazol-2-yl



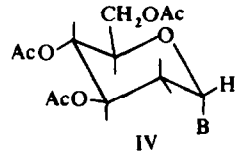
II

IIa B = Benzotriazol-1-yl
IIb B = 5,6-Dimethylbenzotriazol-1-yl
IIc B = 5,6-Dichlorobenzotriazol-1-yl
IId B = 6-Chloropurin-9-yl
IIe B = Benzotriazol-2-yl
IIf B = 5,6-Dimethylbenzotriazol-2-yl
IIg B = 5,6-Dichlorobenzotriazol-2-yl



III

IIIb B = 5,6-Dimethylbenzotriazol-1-yl
IIId B = 6-Chloropurin-9-yl



IV

IVb B = 5,6-Dimethylbenzotriazol-1-yl
IVd B = 6-Chloropurin-9-yl

FIG 1

substitution on the heterocyclic bases was established by UV spectroscopy, and it was confirmed by the appearance of the pattern of the aromatic protons in the NMR spectra. Absorption maxima and extinction coefficients of these substances were in the range of those reported for 1- and 2-alkylbenzotriazole derivatives and 6-chloro-9-methylpurine as listed in Table 1.

TABLE 1

Compound	λ_{max}^{EtOH}	ε
1-Methylbenzotriazole[3]	255	6457
	283	4786
2-Methylbenzotriazole[3]	275	7943
1,5,6-Trimethylbenzotriazole[4]	265*	6850
	286*	5200
2,5,6-Trimethylbenzotriazole[4]	284	10,800
	293	9000
1-Methyl-5,6-dichlorobenzotriazole[5]	268 (sh)	4786
	272	5012
	295	4169
2-Methyl-5,6-dichlorobenzotriazole[5]	286	7762
	293	8913
	300 (sh)	6918
6-Chloro-9-methylpurine[1]	265	9100

* Data from our laboratory.

The magnetic parameters obtained by first-order analysis of the NMR spectra of compounds Ia–f (β-anomers) and IIa–g (α-anomers) are shown in Table 2. Second-order effects such as those arising in part X of an ABX system involved in more complex system have been taken into account. For some complex multiplets not amenable to first-order analysis (e.g. H-5′ and H-6′; H-1′, H-2′ and H-3′) trial calculations were performed using the non-iterative NMRIT program in order to obtain the parameters that best fitted the observed patterns. Errors in chemical shifts and coupling constants may be evaluated as ±0·02 ppm and ±0·5 Hz, respectively.

A complete iterative analysis of the NMR spectra of Id and IId was performed by using the NMRIT and NMREN programs. For each compound the total 7-spin system was subdivided in two 4-spin systems (H-1′, H-2′, H-3′, H-4′ and H-4′, H-5′, H-6′a, H-6′e) which were analysed separately. A total of about 45 lines were measured for each compound. The mean deviation between observed and calculated line frequencies was ±0·10 Hz, and maximum errors for chemical shifts and coupling constants were of ±0·01 ppm and ±0·2 Hz, respectively. Errors in the sub-system H-4′, H-5′, H-6′a, H-6′e of IId were larger (±0·02 ppm and 0·5 Hz), owing to the strong coupling between H-5′, H-6′a and H-6′e.

Coupling constant values obtained for the N-glycosyl compounds listed in Table 2 at once reveal that the sugar moiety in these derivatives is in the half-chair Hl conformation. The value of $J_{4',5'}$ (∽8·5 Hz) is indicative of a *quasi*-axial–axial relationship between H-4′ and H-5′. In addition, the values obtained for $J_{3',4'}$ (1·6–2·1 Hz) are in support of H-4′ being *quasi*-axial (a value of $J_{3',4'} \simeq 6$ Hz would have been obtained for a *quasi*-equatorial arrangement of H-4′). Anomeric configuration has been assigned on the basis of the values of $J_{1',2'}$ and the homoallylic coupling $J_{1',4'}$. The compounds showing the largest homoallylic coupling have been identified as the β-anomers (*quasi*-axial H-1′), in agreement with reported data for conduritols.[6] On the other hand, these configurational assignments was confirmed by the values of $J_{1',2'}$ which show an angular dependence in qualitative agreement with that shown by $J_{3',4'}$ and with the trend of the modified Karplus equation for C(sp³)-C(sp²) fragments.[7] In Table 2 the magnetic parameters of 9-(4,6-di-O-acetyl-2,3-dideoxy-β-D-*erythro*-hex-2-enopyranosyl)-2,6-dichloropurine (Ih) and its α-isomer (IIh), recently prepared by Ferrier and Ponpipom[2g] by fusion of tri-O-acetyl-D-glucal with 2,6-dichloropurine in which the sugar moiety adopts the Hl conformation, are also included for comparison. The great resemblance that exists between the magnetic parameters of the 2,6-dichloropurine derivatives and those of our own N-glycosyl derivatives, justifies the configurational and conformational assignments made.

Table 3 lists the PMR parameters obtained by first-order analysis for compounds IVb and IVd. The assignment to IVb of the Cl conformation is based on the magnitudes of the coupling constants $J_{4',5'} = 9{\cdot}4$ Hz, $J_{3',4'} = 11{\cdot}0$ Hz and $J_{2'a,3'} = 9{\cdot}2$ Hz which indicate an axial disposition for these protons. The anomeric configuration is given by the values of the coupling constants $J_{1',2'a} = 5{\cdot}4$ Hz and $J_{1',2'e} = 1{\cdot}8$ Hz which are characteristics for axial–equatorial and equatorial–equatorial arrangements, respectively. Accordingly the anomeric proton is in an equatorial orientation and therefore the anomeric configuration is α. The conformation of IVd will be discussed later.

With regard to compounds IIIb and IIId, the magnetic parameters of which are also included in Table 3, the sugar conformation was revealed as being Cl by a

TABLE 2. NMR PARAMETERS OF 4',6'-DI-O-ACETYL-2',3'-DIDEOXY-D-*erythro*-HEX-2'-ENOPYRANOSYL DERIVATIVES (60 MHz)

Chemical shifts (τ values)

Compound	Anom.	Solv.	H-1'	H-2'	H-3'	H-4'	H-5'	H-6'	H-6'	Base	CH_3	OAc
Ia	β	$CDCl_3$	3·05	3·80	3·74	4·43	—	5·75	—	1·83–2·83		7·84 8·03
Ib	β	$CDCl_3$	3·14	3·79	3·76	4·45	—	5·76	—	2·27 2·62	7·62	7·84 8·02
Ic	β	$CDCl_3$	3·07	3·83	3·66	4·40	—	5·73	–	1·89 2·22		7·82 7·94
Id*	β	$CDCl_3$	3·24	3·89	3·70	4·44	5·78	5·72	5·74	1·16 1·68		7·82 7·92
If	β	$CDCl_3$	3·30	3·78	3·73	4·51	—	5·79	—	——2·41——	7·62	7·88 8·05
IIa	α	$CDCl_3$	3·36	3·64	3·61	4·46	6·08	5·74	5·97	1·82–2·65		7·88 8·07
IIb	α	$CDCl_3$	3·44	3·70	3·64	4·48	6·03	5·74	5·98	2·17 2·51	7·55	7·87 8·04
IIc	α	$CDCl_3$	3·43	3·66	3·56	4·53	6·12	5·74	5·92	1·83 2·06		7·86 8·01
IId*	α	$CDCl_3$	3·35	3·76	3·60	4·52	6·05	5·75	5·90	1·18 1·67		7·85 8·08
IIe	α	$CDCl_3$	3·25	3·77	3·69	4·42	5·55	5·85	5·70	1·98–2·26		7·85 7·97
IIf	α	$CDCl_3$	3·33	3·79	3·72	4·46	5·58	5·73	5·89	——2·35——	7·59	7·87 7·99
IIf	α	C_6D_6	3·35	4·30	3·94	4·28	5·22	5·66	5·84	——2·32——	7·91	8·24 8·33
IIg	α	$CDCl_3$	3·32	3·86	3·63	4·44	5·60	——5·76——		——1·94——		7·83 7·95
Ih*	β	C_6D_6	4·02	4·87	4·25	4·63	6·38	——5·9 ——		2·42		
IIh*	α	$CDCl_3$	3·42	3·81	3·60	4·58	6·08	——5·8 ——		1·71		

Coupling constants (Hz)

Compound	Anom.	Solv.	$J_{1',2'}$	$J_{1',3'}$	$J_{1',4'}$	$J_{2',3'}$	$J_{2',4'}$	$J_{3',4'}$	$J_{4',5'}$	$J_{5',6'}$	$J_{5',6'}$	$J_{6',6'}$
Ia	β	$CDCl_3$				11·5						
Ib	β	$CDCl_3$				11·6						
Ic	β	$CDCl_3$				11·5			8·4			
Id	β	$CDCl_3$	1·8	−2·2	2·6	10·2	−1·6	1·8	8·4	4·7	3·3	−12·2
If	β	$CDCl_3$	1·9			11·4						
IIa	α	$CDCl_3$				10·6			8·9	5·8	2·6	−12·8
IIb	α	$CDCl_3$				10·6		1·6	8·8	6·0	2·9	−12·4
IIc	α	$CDCl_3$				10·9			8·3	6·2	2·1	−12·2
IId	α	$CDCl_3$	3·0	−2·0	1·6	10·2	−2·0	2·0	9·0	5·3	2·6	−12·1
IIe	α	$CDCl_3$				11·6			8·7	3·9	2·9	−12·4
IIf	α	C_6D_6	2·8	−1·3	1·8	10·3	−1·9	2·1	9·8	4·8	2·2	−12·4
IIg	α	$CDCl_3$				11·1			8·2			
Ih	β	C_6D_6	1·5	2·0	2·2	10·0	2·2	2·0	9·0			
IIh	α	$CDCl_3$	3·0	1·5	1·2	10·0	1·7	1·7	8·5			

* 100 MHz.

TABLE 3. NMR PARAMETERS OF 3',4',6'-TRI-O-ACETYL-2'-DEOXY-D-*arabino*-HEXOPYRANOSYL DERIVATIVES (60 MHz)

Chemical shifts (τ values)

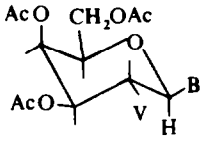
Compound	Anom.	Solvent	H-1'	H-2'a	H-2'e	H-3'	H-4'	H-5'	H-6'	H-6''	Base		CH_3		OAc		
IIIb	β	$CDCl_3$	3·86	—7·24—		—4·74—		5·96	5·70	5·83	2·25	2·60	7·58	7·62	7·92—		—7·95—
IIIb	β	C_6D_6	4·19	—7·40—		—4·60—		6·02	5·60	5·80	2·14	2·59	7·83	7·88	8·14—		—8·23—
IIId	β	$CDCl_3$	3·91	7·48	7·23	4·70	4·78	5·97	5·65	5·81	1·18	1·58			7·88—		—7·91—
IVb	α	$CDCl_3$	3·69	7·11	6·73	4·28	5·01	6·59	5·75	6·10	2·24	2·57	—7·60—		7·95—		—8·00—
IVd	α	$CDCl_3$	3·65	7·54	6·65	4·55	4·91	6·08	5·57	6·00	1·19	1·57			7·85	7·90	7·93

Coupling constants (Hz)

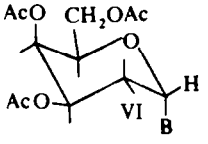
Compound	Anom.	Solvent	$J_{1',2'a}$	$J_{1',2'e}$	$J_{2'a,2'e}$	$J_{2'a,3'}$	$J_{2'e,3'}$	$J_{3',4'}$	$J_{4',5'}$	$J_{5',6'}$	$J_{5',6''}$	$J_{6',6''}$
IIIb	β	C_6D_6	Sum 13·6						9·6	4·4	2·1	−12·5
IIId	β	$CDCl_3$	11·0	2·5	−12·7	12·0	4·2	9·0	9·0	6·1	2·2	−12·6
IVb	α	$CDCl_3$	5·4	1·8	−14·0	9·2	5·6	11·0	9·4	4·9	2·3	−12·5
IVd	α	$CDCl_3$	5·1	4·5	−14·3	7·9	5·3	6·5	6·7	7·0	3·5	−12·8

characteristic diaxial coupling between H-4′ and H-5′ with $J_{4',5'} = 9{\cdot}0$–$9{\cdot}6$ Hz. In the case of IIIb it was not possible to obtain any coupling constant from the multiplet at 4·74 τ ($CDCl_3$) assigned to H-3′ and H-4′. A quartet at 3·86 τ and a multiplet at 7·24 τ ($CDCl_3$) were assigned to H-1′ and to the two protons bonded to C-2′, respectively. These protons form an ABX system further involved by coupling to H-3′, in which the difference $[\tau_A - \tau_B]$ is close to zero. Since part AB is not amenable to analysis and the outer lines in the X part are missing we can only get from the spectrum the value of the sum $[J_{1',2'a} + J_{1',2'e}] = 13{\cdot}6$ Hz. This large value suggest the existence of a diaxial coupling, and therefore compounds IIIb and IIId have the β-D-anomeric configuration.

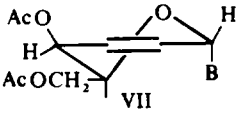
Reaction of tri-O-acetyl-D-galactal with the same bases under exactly the same experimental conditions, afforded almost exclusively the corresponding 2-deoxy-hexopyranosyl derivatives Va–d and VIa–g (Fig 2). Only in two cases (VIIa, c) 2′,3′-



Va B = Benzotriazol-1-yl
Vb B = 5,6-Dimethylbenzotriazol-1-yl
Vc B = 5,6-Dichlorobenzotriazol-1-yl
Vd B = 6-Chloropurin-9-yl



VIa B = Benzotriazol-1-yl
VIb B = 5,6-Dimethylbenzotriazol-1-yl
VIc B = 5,6-Dichlorobenzotriazol-1-yl
VId B = 6-Chloropurin-9-yl
VIe B = Benzotriazol-2-yl
VIf B = 5,6-Dimethylbenzotriazol-2-yl
VIg B = 5,6-Dichlorobenzotriazol-2-yl



VIIa B = Benzotriazol-1-yl
VIIc B = 5,6-Dichlorobenzotriazol-1-yl

FIG 2

unsaturated products were isolated. Comparison of the UV spectra of all the N-glycosyl derivatives obtained with those of suitable model compounds (Table 1) allowed us to establish the site of glycosidation.

PMR parameters obtained for compounds Va–d (β-anomers) and VIa–g (α-anomers) are given in Table 4. In the following discussion we will refer to Vc and VIc as representative compounds of both sets of anomers, and the conclusions drawn may be applied to the other N-glycosyl derivatives as well. On the other hand, despite the fact that the configurations and conformations of the N-2 (VIe–g) and the N-1 (VIa–c) glycosyl derivatives are the same we discuss them separately since there are differences in their respective NMR spectra.

A complete analysis of the NMR spectra of Vc and VIc was performed using the NMRIT and NMREN programs. The total system was subdivided as above. A total

TABLE 4. NMR PARAMETERS OF 3',4',6'-TRI-O-ACETYL-2'-DEOXY-D-*lyxo*-HEXOPYRANOSYL DERIVATIVES (60 MHz)

Chemical shifts (τ values. Deuteriochloroform)

Compound	Anom.	H-1'	H-2'a	H-2'e	H-3'	H-4'	H-5'	H-6'	H-6'	Base	CH_3	OAc		
Va	β	3·72	7·00	7·54	4·66	4·49	—	5·77	—	1·77–2·74		7·75	—7·95—	
Vb	β	3·83	6·99	?	4·70	4·51	—	5·79	—	2·17 2·51	7·56	7·74	—7·94—	
Vc	β	3·78	7·18	7·39	4·71	4·52	—	5·78	—	1·82 2·07		7·73	7·91	7·96
Vd	β	3·90	7·64	7·85	4·68	4·60		5·80		1·28 1·60		7·78	—7·96—	
VIa	α	3·50	7·30	6·95	4·23	4·60	6·42	5·91	5·98	1·84–2·68		7·80	7·97	8·13
VIb	α	3·59	7·34	6·97	4·15	4·55	6·37	5·85	5·94	2·16 2·50	7·55	7·79	7·95	8·09
VIc*	α	3·57	7·32	6·89	4·39	4·61	6·39	5·85	5·96	1·83 2·05		7·80	7·97	8·00
VId	α	3·62	7·38	6·77	4·52	4·60	5·89	5·64	5·88	1·29 1·59		7·81	7·93	7·98
VIe	α	3·39	—7·35—		3·93	4·49	—	5·85	—	2·03–2·75		7·80	7·96	8·03
VIf	α	3·43	—7·39—		3·87	4·49	—	5·87	—	—2·38—	7·58	7·80	7·95	8·03
VIg	α	3·42	—7·37—		4·04	4·52	—	5·86	—	—1·98—		7·78	7·95	8·01

Coupling constants (Hz)

Compound	Anom.	$J_{1',2'a}$	$J_{1',2'e}$	$J_{1',5'}$	$J_{2'a,2'e}$	$J_{2'a,3'}$	$J_{2'e,3'}$	$J_{2'e,4'}$	$J_{3',4'}$	$J_{4',5'}$	$J_{5',6'}$	$J_{5',6'}$	$J_{6',6'}$
Va	β	11·1	3·1		−12·5	11·3	5·0		2·9				
Vb	β	10·7	2·6		−14·3	11·5	5·6		2·7				
Vc	β	11·2	2·6		−13·1	12·2	5·3		3·1	~1			
Vd	β	11·3	2·3		−12·6	12·0	4·7		2·8	1·3			
VIa	α	4·9	1·3	~1	−13·2	11·8	5·8	~1	3·1	1·0	7·1	5·0	−10·1
VIb	α	5·4	1·5		−13·7	12·1	5·9		3·4	1·3	7·8	5·3	−11·2
VIc*	α	5·4	1·2	1·3	−13·7	12·5	5·1	1·0	3·2	1·9	8·0	4·3	−11·5
VId	α	4·8	2·7		−13·8	10·3	5·0		3·2	1·0	8·7	4·0	−12·4
VIe	α	Sum 7·2			?	Sum 17·8			3·1				
VIf	α	Sum 7·6			?	Sum 17·5			3·2				
VIg	α	Sum 6·7			?	Sum 16·8			3·2				

* 100 MHz.

of about 65–70 lines were measured for each compound; the mean deviation between the observed and calculated frequencies is ±0·06 Hz and the maximum errors for the chemical shifts and coupling constants are ±0·01 ppm and ±0·1 Hz, respectively.

The magnitude of the coupling constants $J_{2'a,3'} = 12·2$ Hz and $J_{2'e,3'} = 5·3$ Hz in the case of Vc, and $J_{2'a,3'} = 12·5$ Hz and $J_{2'e,3'} = 5·1$ Hz for VIc suggest that H-3′ occupies an axial position and therefore that both compounds adopt the Cl conformation. The anomeric proton of Vc appears at 3·78 τ as a quartet with $J_{1',2'a} = 11·2$ Hz and $J_{1',2'e} = 2·6$ Hz. These values of the coupling constants are consistent with an axial orientation of H-1′, and indicate the β-anomeric configuration of Vc. Similarly, the assignment of an α-anomeric configuration to VIc is based on the magnitude of the coupling constants $J_{1',2'a} = 5·4$ Hz and $J_{1',2'e} = 1·2$ Hz as determinated in the quartet at 3·57 τ.

Table 4 includes the magnetic parameters obtained from the NMR spectra of the N-2 glycosylbenzotriazoles (VIe–g). As all these spectra are very similar we will refer to compound VIg and the conclusions drawn can be applied to the remaining products. The narrow multiplet at 7·37 τ is assigned to H-2′ protons. Due to accidental degeneracy these protons behave as magnetically equivalent, and this makes the anomeric proton to appear as a pseudo-triplet (3·42 τ). From this signal only the sum $[J_{1',2'a} + J_{1',2'e}] = 6·7$ Hz can be determined which is sufficient to establish that H-1′ is equatorialy oriented (a value of 14 Hz can be expected for an axial H-1′ as in Vc). The multiplet centered at 4·04 τ is assigned to H-3′. The value of the sum $[J_{2'a,3'} + J_{2'e,3'}] = 16·8$ Hz is large enough to allow the existence of a diaxial coupling between H-3′ and H-2′a. All these conclusions clearly support the Cl conformation and the α-anomeric configuration of VIg.

The NMR spectra of the 2′,3′-unsaturated compounds derived from D-galactal VIIa and VIIc (Fig 2) present close similarities as well (Table 5). As in the previous cases we only refer to the NMR spectrum of one of these products (VIIa). In $CDCl_3$ the accidental overlap of the signals due to H-1′, H-2′ and H-3′ on one hand and H-5′ and H-6′ on the other precluded any analysis. Partial analysis was possible when

TABLE 5. NMR PARAMETERS OF 4′,6′-DI-O-ACETYL-2′,3′-DIDEOXY-α-D-*threo*-HEX-2′-ENOPYRANOSYL DERIVATIVES (60 MHz)

Chemical shifts (τ values)

Compound	Solvent	H-1′	H-2′	H-3′	H-4′	H-5′	H-6′	H-6′	Base	OAc	
VIIa	$CDCl_3$	—	3·37	—	4·71	—	5·83	—	1·74–2·60	7·96	8·20
VIIa	C_6D_6	3·94	3·91	3·71	4·95	5·96	——5·84——		1·74–3·00	8·25	8·45
VIIc	$CDCl_3$	—	3·43	—	4·78	—	5·86	—	1·81 2·08	7·85	8·15

Coupling constants (Hz)

Compound	Solvent	$J_{1',2'}$	$J_{1',3'}$	$J_{2',3'}$	$J_{3',4'}$	$J_{4',5'}$
VIIa	C_6D_6	2·6	2·1	11·0	4·8	2·2
VIIc	$CDCl_3$	—	—	—	—	—

hexadeuteriobenzene was used. The quartet centered at 4·95 τ was assigned to H-4′. The magnitude of the observed coupling constant $J_{3',4'} = 4{\cdot}8$ Hz is consistent with a *quasi*-equatorial orientation of H-4′; further, the magnitude of the coupling constant $J_{4',5'} = 2{\cdot}2$ Hz is also consistent with a *quasi*-equatorial–axial coupling. Consequently the N-glycosylbenzotriazole VIIa preferentially adopts the Hl conformation. The anomeric configuration of this compound was easily determined from the values of the vicinal and homoallylic coupling constants $J_{1',2'} = 2{\cdot}6$ Hz, and $J_{1',4'} = 0$ Hz, respectively, which are indicative of a *quasi*-equatorial disposition of H-1′.[8]

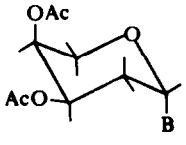
The NMR spectra of the purine derivatives 9-(3,4,6-tri-O-acetyl-2-deoxy-α-D-*arabino*-hexopyranosyl)-6-chloropurine (IVd) and 9-(3,4,6-tri-O-acetyl-2-deoxy-α-D-*lyxo*-hexopyranosyl)-6-chloropurine (VId) present some differences with regard to those of the N-glycosylbenzotriazoles IV and VI. Coupling constant of these latter compounds are in satisfactory agreement for a pure Cl conformation.[9] From the comparison of the observed values for $[J_{1',2'a} + J_{1',2'e}]$, $[J_{2'a,3'} + J_{2'e,3'}]$, $J_{3',4'}$ and $J_{4',5'}$ of IVd and VId with the correspondingly observed for compounds IVb and VIa–c (Table 6) it is clear that the former values deviate from the latter ones in a

TABLE 6

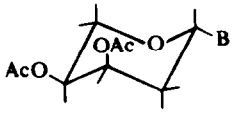
Compound	$J_{1',2'a} + J_{1',2'e}$	$J_{2'a,3'} + J_{2'e,3'}$	$J_{3',4'}$	$J_{4',5'}$
IVd	9·6	13·2	6·5	6·7
IVb	7·2	14·8	11·0	9·4
VId	7·5	15·3		
VIa, b, c (average)	6·5	17·7		

larger proportion than attributable to experimental errors. This is particularly obvious in the case of the coupling constants $J_{3',4'}$ and $J_{4',5'}$ for IVd.

All these observed deviations can be explained admitting that a small proportion of the alternative 1C conformers of IVd and VId are present in equilibrium with the favoured Cl forms. Nevertheless, it is noteworthy that in the 1C conformation the acetoxy–methyl group at C-5′ is axially oriented. The existence of this equilibrium implies that the 6-chloro-9-purinyl moiety has a strong predisposition for an equatorial position. Although reason for this stereochemical preference is not clear, it can be attributed to the effect of the unfavourable interactions which exist in the Cl conformation between the H-8 proton of the purine and the H-3′ and H-5′ hydrogen atoms of the sugar, as is apparent from the molecular models.



C1(L),β
B = Benzotriazolyl
VIII



1C(L),β
B = 6-Chloro-9-purinyl
IX

FIG 3

The fact that this interaction may play a role in determining the sugar conformation is confirmed by the conclusions obtained from prior studies[2e,f] on the reactions of 3,4-di-O-acetyl-L-arabinal with several benzotriazoles and 6-chloropurine. There, it was shown that whereas the benzotriazole derivatives VIII (β-anomers) (Fig 3) showed a small preference for the Cl (L) conformation (50–60%), in the case of the 6-chloro-9-(3,4-di-O-acetyl-2-deoxy-β-L-*erythro*-pentopyranosyl)purine (IX) the conformational equilibrium was strongly shifted towards the 1C (L) conformation (90%).

EXPERIMENTAL

M.ps are uncorrected. UV absorption spectra were taken with a Perkin–Elmer 350 spectrophotometer. NMR spectra were recorded with Perkin–Elmer R-10 and Varian HA-100 spectrometers, in 10–15% w/v solutions at standard probe temp, TMS being used as an internal reference. Optical rotations were measured with a Perkin–Elmer 141 polarimeter. Preparative layer chromatography (20 × 20 cm, 2 mm thickness) was performed on PF_{254} silica gel (Merck): silica gel GF_{254} (Merck) was used for analytical TLC. Spots were visualized with UV light (254 mμ).

Reaction of 3,4,6-*tri*-O-*acetyl*-D-*glucal with benzotriazole*

A mixture of benzotriazole (1·19 g, 0·01 mole) and the glycal (5·44 g, 0·02 mole) in pure EtOAc (70 ml) with a few drops of trifluoracetic acid was heated in a sealed tube under continuous agitation at 90°. After 39 hr the solvent was evaporated *in vacuo* and the residue was dissolved in $CHCl_3$ and applied to 25 preparative TLC plates. The plates were developed 16 times with a mixture of ether–light petroleum (3:4). Under UV light three major bands were visible, which were removed and the compounds extracted with EtOAc.

1-(4,6-*Di*-O-*acetyl*-2,3-*dideoxy*-β-D-erythro-*hex*-2-*enopyranosyl*)*benzotriazole* (Ia). The slowest running band gave 0·6 g of a syrup which was rechromatographed to pure Ia, $[\alpha]_D$ +199·2° (*c* 0·3, $CHCl_3$): λ_{max}^{EtOH} 254 (ε, 7600), 259 (ε, 7450), 279 mμ (ε, 5850). (Found: C, 58·23; H, 5·44; N, 12·38. $C_{16}H_{17}N_3O_5$ requires: C, 58·00; H, 5·17; N, 12·68%).

1-(4,6-*Di*-O-*acetyl*-2,3-*dideoxy*-α-D-erythro-*hex*-2-*enopyranosyl*)*benzotriazole* (IIa). The second band gave 0·8 g of a solid IIa, m.p. 122–123° (from EtOH), $[\alpha]_D$ +127·2 (*c* 1, $CHCl_3$); λ_{max}^{EtO} 253 (ε, 7210), 259 (ε, 6670) (sh), 280 mμ (ε, 4140). (Found: C, 58·39; H, 5·25; N, 12·59. $C_{16}H_{17}N_3O_5$ requires: C, 58·00; H, 5·17; N, 12·68%).

2-(4,6-*Di*-O-*acetyl*-2,3-*dideoxy*-α-D-erythro-*hex*-2-*enopyranosyl*)*benzotriazole* (IIe). The third band afforded 0·5 g of a solid which was crystallized from MeOH to give IIe, m.p. 127–128°, $[\alpha]_D$ −96·6° (*c* 1, $CHCl_3$): λ_{max}^{EtOH} 274 (ε, 14,000), 278 mμ (ε, 14,200). (Found: C, 58·30; H, 5·26; N, 12·88. $C_{16}H_{17}N_3O_5$ requires: C, 58·00; H, 5·17; N, 12·68%).

Reaction of 3,4,6-*tri*-O-*acetyl*-D-*glucal with* 5,6-*dimethylbenzotriazole*

Tri-acetil-D-glucal (9·52 g, 0·035 mole) and 5,6-dimethylbenzotriazole (3·67 g, 0·025 mole) in EtOAc (150 ml) containing trifluoracetic acid (6–8 drops) were heated for 4 days as in the preceding case. The crude thick syrup obtained was dissolved in a small amount of EtOAc and applied to 40 preparative TLC plates which were eluted 9 times with ether–light petroleum (1:1), resulting in the separation of the following seven compounds:

1-(3,4,6-*Tri*-O-*acetyl*-2-*deoxy*-β-D-arabino-*hexopyranosyl*)-5,6-*dimethylbenzotriazole* (IIIb). The slower moving band gave 0·2 g of as a fairly heat sensitive solid. This product was purified by preparative TLC (same solvent system as above); the compound so obtained was dissolved in a minimum volume of benzene and the soln was treated with light petroleum till turbidity. The soln was allowed to stand in the refrigerator for 20 min, and the colourless crystals which formed were filtered, m.p. 132–133°, $[\alpha]_D$ −31·2° (*c* 0·6, $CHCl_3$); λ_{max}^{EtOH}, 260 (ε, 7100), 286 mμ (ε, 4250). (Found: C, 57·20; H, 5·96; N, 9·81. $C_{20}H_{25}N_3O_7$ requires: C, 57·27; H, 6·00; N, 10·01%).

1-(3,4,6-*Tri*-O-*acetyl*-2-*deoxy*-α-D-arabino-*hexopyranosyl*)-5,6-*dimethylbenzotriazol* (IVb). The second band gave 0·24 g of IVb which was recrystallized from EtOAc–light petroleum as in the preceding case in order to avoid its transformation in IIb. Pure product had m.p. 137–138°, $[\alpha]_D$ +172·2° (*c* 0·5 $CHCl_3$);

λ_{max}^{EtOH}, 261 (ε, 5200), 266 (ε, 4900) (sh), 284 mμ (ε, 3050). (Found: C, 57·27; H, 5·89; N, 9·79. $C_{20}H_{25}N_3O_7$ requires: C, 57·27; H, 6·00, N, 10·01%).

1-(4,6-*Di*-O-*acetyl*-2,3-*dideoxy*-β-D-erythro-*hex*-2-*enopyranosyl*)-5,6-*dimethylbenzotriazole* (Ib). Extraction of the next band using ether as solvent and evaporation *in vacuo*, gave 0·6 g of a solid material which easily converted into IIb. A NMR spectra of a fresh $CDCl_3$ soln showed the product to be a mixture of Ib (~70%) and the unsaturated compound IIb.

1-(4,6-*Di*-O-*acetyl*-2,3-*dideoxy*-α-D-erythro-*hex*-2-*enopyranosyl*)-5,6-*dimethylbenzotriazole* (IIb). The fourth band was formed by 0·5 g of IIb, which was recrystallized from EtOAc–light petroleum, m.p. 162–163°, $[\alpha]_D$ +149·4° (*c* 1, $CHCl_3$); λ_{max}^{EtOH}, 260 (ε, 7500), 266 (ε, 7200), 290 mμ (ε, 4100). (Found: C, 60·04; H, 6·07; N, 11·89. $C_{18}H_{21}N_3O_5$ requires: C, 60·15; H, 5·84; N, 11·69%).

5,6-*Dimethylbenzotriazole*. The following band afforded 1 g of 5,6-dimethylbenzotriazole identical with an authentic sample.

2-(4,6-*Di*-O-*acetyl*-2,3-*dideoxy*-β-D-erythro-*hex*-2-*enopyranosyl*)-5,6-*dimethylbenzotriazole* (If). The next band gave 0·32 g of If m.p. 154–155° (from EtOAc–light petroleum) $[\alpha]_D$ +211·8° (*c* 1, $CHCl_3$); λ_{max}^{EtOH}, 279 (ε, 12,250) (sh), 284 (ε, 13,850), 296 mμ (ε, 11,500). (Found: C, 60·36, H, 5·92, N, 11·54. $C_{18}H_{21}N_3O_5$ requires: C, 60·15; H, 5·84; N, 11·69%).

2-(4,6-*Di*-O-*acetyl*-2,3-*dideoxy*-α-D-erythro-*hex*-2-*enopyranosyl*)-5,6-*dimethylbenzotriazole* (IIf). The fastest moving band afforded 0·86 g of IIf, m.p. 132–133° (from EtOAc–light petroleum) $[\alpha]_D$ −98·5° (*c* 1, $CHCl_3$); λ_{max}^{EtOH}, 277 (ε, 10,050) (sh), 284 (ε, 11,900), 295 mμ (ε, 9800). (Found: C, 60·38; H, 6·07; N, 11·87. $C_{18}H_{21}N_3O_5$ requires: C, 60·15; H, 5·84; N, 11·69%).

Reaction of 3,4,6-*tri*-O-*acetyl*-D-*glucal with* 5,6-*dichlorobenzotriazole*

The glycal (8·5 g, 0·032 mole) and 5,6-dichlorobenzotriazole (4 g, 0·021 mole) in 150 ml of EtOAc were heated for 4 days under the same experimental conditions above indicated. The crude product was dissolved in hot benzene and the soln was allowed to stand at room temp for 24 hr. The crystallized 5,6-dimethylbenzotriazole was removed by filtration and the filtrated concentred *in vacuo* to a syrup. Preparative TLC (35 plates) of this material using ether–light petroleum (1:3) as eluent (10 developments) resulted in the separation of 3 fractions.

1-(4,6-*Di*-O-*acetyl*-2,3-*dideoxy*-β-D-erythro-*hex*-2-*enopyranosyl*)-5,6-*dichlorobenzotriazole* (Ic). Elution of the slowest band afforded 1·2 g of crystalline Ic, m.p. 102–103° (from MeOH), $[\alpha]_D$ +207·4° (*c* 1, $CHCl_3$); λ_{max}^{EtOH}, 262 (ε, 9690), 268 (ε, 6500) (sh), 296 (ε, 4730), 303 mμ (ε, 3790) (sh). (Found: C, 48·09; H, 3·83; N, 10·65. $C_{16}H_{15}Cl_2N_3O_5$ requires: C, 48·00; H, 3·75; N, 10·50%).

1-(4,6-*Di*-O-*acetyl*-2,3-*dideoxy*-α-D-erythro-*hex*-2-*enopyranosyl*)-5,6-*dichlorobenzotriazole* (IIc). The second band gave 1·2 g of IIc, m.p. 113–114° (from MeOH), $[\alpha]_D$ +177·7° (*c* 1, $CHCl_3$); λ_{max}^{EtOH}, 263 (ε, 7200), 270 (ε, 6750) (sh), 296 (ε, 4540), 304 mμ (ε, 2940) (sh). (Found: C, 48·08; H, 3·83; N, 10·60. $C_{16}H_{15}Cl_2N_3O_5$ requires: C, 48·00; H, 3·75; N, 10·50%).

2-(4,6-*Di*-O-*acetyl*-2,3-*dideoxy*-α-D-erythro-*hex*-2-*enopyranosyl*)-5,6-*dichlorobenzotriazole* (IIg). The fastest band gave 0·77 g of IIg, m.p. 137–138° (from MeOH), $[\alpha]_D$ −115·3° (*c* 1, $CHCl_3$); λ_{max}^{EtOH}, 287 (ε, 11,500) (sh), 295 (ε, 19,300), 305 mμ (ε, 13,000). (Found: C, 47·77; H, 3·67; N, 10·25. $C_{16}H_{15}Cl_2N_3O_5$ requires: C, 48·00; H, 3·75; N, 10·50%).

Reaction of 3,4,6-*tri*-O-*acetyl*-D-*glucal with* 6-*chloropurine*

A mixture of tri-O-acetil-D-glucal (5·44 g, 0·02 mole) and 6-chloropurine (1·55 g, 0·01 mole) in 50 ml EtOAc was heated 24 hr as in the preceding cases. The crude mixture (6·04 g) was separated into 3 fractions by preparative TLC (19 plates) after 19 consecutive developments using ether–light petroleum (2:1).

6-*Chloro*-9-(4,6-*di*-O-*acetyl*-2,3-*dideoxy*-β-D-erythro-*hex*-2-*enopyranosyl*)*purine* (Id). Elution of the fastest band followed by rechromatography using ether–light petroleum (3:1) (15 developments) gave 0·34 g of crystalline Id, m.p. 110° (from EtOAc–light petroleum), $[\alpha]_D$ +85·6° (*c* 0·6, $CHCl_3$); λ_{max}^{EtOH}, 263 mμ (ε, 8625). (Found: C, 48·89; H, 3·94; N, 15·05; Cl, 9·78. $C_{15}H_{15}ClN_4O_5$ requires: C, 49·12; H, 4·09; N, 15·28; Cl, 9·66%).

6-*Chloro*-9-(4,6-*di*-O-*acetyl*-2,3-*dideoxy*-α-D-erythro-*hex*-2-*enopyranosyl*)*purine* (IId). Extraction of the second band followed by rechromatography using EtOAc–light petroleum (1:1) (7 developments) gave 0·68 g of IId, m.p. 85–86° (from EtOAc–light petroleum), $[\alpha]_D$ +59·9° (*c* 1, $CHCl_3$); λ_{max}^{EtOH}, 264 mμ (ε, 9450). (Found: C, 48·83; H, 4·23; N, 14·99; Cl, 9·92. $C_{15}H_{15}ClN_4O_5$ requires: C, 49·12; H, 4·09; N, 15·28; Cl, 9·66%).

6-*Chloro*-9-(3,4,6-*tri*-O-*acetyl*-2-*deoxy*-β- *and* α-D-arabino-*hexopyranosyl*)*purine* (IIId) *and* (IVd). Elution

of the slowest band followed by chromatography using ether as developer gave two bands. The slower moving of these gave 6-chloropurine. The other one gave 0·27 g of a syrup. Rechromatography of this material using EtOAc–light petroleum (1:1) (20 developments) separated it into two compounds. The fast moving band gave 0·08 g of IIId, m.p. 143–144° (from EtOAc–light petroleum), $[\alpha]_D$ −18·9° (*c* 0·8, $CHCl_3$); λ_{max}^{EtOH}, 264 mμ (ε, 7920). (Found: C, 47·53; H, 4·55; N, 12·87; Cl, 8·48. $C_{17}H_{19}ClN_4O_7$ requires: C, 47·84; H, 4·45; N, 13·13; Cl, 8·30%).

The slow band gave 0·17 g of as a syrup IVd which could not be crystallized, $[\alpha]_D$ +52·6° (*c* 0·5, $CHCl_3$); λ_{max}^{EtOH}, 264 mμ (ε, 8300). (Found: C, 47·56; H, 4·48; N, 12·89; Cl, 8·49. $C_{17}H_{19}ClN_4O_7$ requires: C, 47·84; H, 4·45; N, 13·13; Cl, 8·30%).

*Reaction of tri-*O*-acetyl-*D*-galactal with benzotriazole*

A mixture of glycal (5·44 g, 0·02 mole) and benzotriazole (1·19 g, 0·01 mole) was heated for 37 hr as in the preceding cases. The crude product obtained was separated into 5 fractions by preparative TLC (27 plates) after 7 consecutive developments using ether–light petroleum (1:1).

1-(3,4,6-*Tri*-O-*acetyl*-2-*deoxy*-β-D-lyxo-*hexopyranosyl*) *benzotriazole* (Va). The slower moving band gave 0·25 g of Va, m.p. 140–141° (from EtOAc–light petroleum), $[\alpha]_D$ −24·1° (*c* 1, $CHCl_3$); λ_{max}^{EtOH}, 253 (ε, 8100), 259 (ε, 7420) (sh), 282 mμ (ε, 5300). (Found: C, 54·99; H, 5·57; N, 10·71. $C_{18}H_{21}N_3O_7$ requires: C, 55·24; H, 5·40; N, 10·74%).

1-(3,4,6-*Tri*-O-*acetyl*-2-*deoxy*-α-D-lyxo-*hexopyranosyl*) *benzotriazole* (VIa). The next band afforded 1·2 g of a syrup which further purified by preparative TLC using EtOAc–$CHCl_3$–light petroleum (1:1:4) as developer (7 developments) giving pure VIa, $[\alpha]_D$ +120·8° (*c* 1, $CHCl_3$), λ_{max}^{EtOH}, 253 (ε, 6950), 259 (ε, 6550) (sh), 279 mμ (ε, 3950). (Found: C, 55·52; H, 5·45; N, 10·99. $C_{18}H_{21}N_3O_7$ requires: C, 55·24; H, 5·40; N, 10·74%).

1-(4,6-*Di*-O-*acetyl*-2,3-*dideoxy*-α-D-threo-*hex*-2-*enopyranosyl*) *benzotriazole* (VIIa). The next band gave 0·33 g of VIIa, m.p. 123–124° (from EtOAc–light petroleum), $[\alpha]_D$ −85·7° (*c* 1, $CHCl_3$); λ_{max}^{EtOH}, 254 (ε, 7450), 260 (ε, 6850) (sh), 282 mμ (ε, 4050). (Found: C, 57·75; H, 5·32; N, 12·60. $C_{16}H_{17}N_3O_5$ requires: C, 58·00; H, 5·17; N, 12·68%).

2-(3,4,6-*Tri*-O-*acetyl*-2-*deoxy*-α-D-lyxo-*hexopyranosyl*) *benzotriazole* (VIe). The next band gave 0·35 g of solid VIe, m.p. 160–161° (from EtOH), $[\alpha]_D$ +90·4° (*c* 1, $CHCl_3$); λ_{max}^{EtOH}, 273 (ε, 11,600), 277 (ε, 11,700), 283 mμ (ε, 10,100) (sh). (Found: C, 55·24; H, 5·66; N, 10·94. $C_{18}H_{21}N_3O_7$ requires: C, 55·24; H, 5·40; N, 10·74%).

2-(4,6-*Di*-O-*acetyl*-1,2,3-*trideoxy*-D-xylo-*hex*-1-*enopyranos*-3-*yl*)*benzotriazole*. The fastest band gave 0·25 g of a syrup which was further purified by TLC using EtOH–$CHCl_3$–light petroleum (1:1:7) as developer system. After 8 consecutive developments a homogeneous syrup was obtained, $[\alpha]_D$ +369·2° (*c* 0·5, $CHCl_3$); λ_{max}^{EtOH}, 274 (ε, 7350), 278 (ε, 7500), 284 mμ (ε, 6450). Its structure was tentatively assigned from an NMR spectrum analysis and it was not further studied. NMR ($CDCl_3$, τ), 3·17 (H-1'), 4·82 (H-2'), 4·60 (H-3'), 4·47 (H-4'), 5·29 (H-5'), 5·73 (H-6'). Coupling constants (Hz) $J_{1',2'}$ = 5·9, $J_{1',3'}$ = 1·0, $J_{2',3'}$ = 4·9, $J_{2',4'}$ = 1·7, $J_{3',4'}$ = 2·0, $J_{4',5'}$ = 1·8. (Found: C, 57·70; H, 5·23; N, 12·81. $C_{16}H_{17}N_3O_5$ requires: C, 58·00; H, 5·17; N, 12·68%).

Reaction of 3,4,6-*tri*-O-*acetyl*-D-*galactal with* 5,6-*dimethylbenzotriazole*

The crude product obtained from reacting the glycal (6·8 g, 0·025 mole) and 5,6-dimethylbenzotriazole (2·2 g, 0·015 mole) for 65 hr at 95° was chromatographed on 33 preparative plates. After 5 consecutive developments with ether–light petroleum (4:3), four major bands were separated.

5,6-*Dimethylbenzotriazole*. The fastest band gave 1·35 g of crystalline 5,6-dimethylbenzotriazole.

1-(3,4,6-*Tri*-O-*acetyl*-2-*deoxy*-β-D-lyxo-*hexopyranosyl*)-5,6-*dimethylbenzotriazole* (Vb). The slowest band afforded a solid compound (0·3 g) which was crystallized from EtOH to give pure Vb, m.p. 155–156°, $[\alpha]_D$ −32·6° (*c* 1, $CHCl_3$); λ_{max}^{EtOH}, 259 (ε, 7000), 264 (ε, 6600) (sh), 287 mμ (ε, 4050). (Found: C, 56·99; H, 6·00; N, 9·87. $C_{20}H_{25}N_3O_7$ requires: C, 57·27; H, 5·96; N, 10·02%).

1-(3,4,6-*Tri*-O-*acetyl*-2-*deoxy*-α-D-lyxo-*hexopyranosyl*)-5,6-*dimethylbenzotriazole* (VIb). The second band gave 1·3 g of a syrup which was further chromatographed using two developments with ether–light petroleum (4:3) giving pure VIb, $[\alpha]_D$ +179·0° (*c* 0·5, $CHCl_3$); λ_{max}^{EtOH}, 261 (ε, 7600), 266 (ε, 7400) (sh), 286 mμ (ε, 4760). (Found: C, 57·31; H, 5·88; N, 10·24. $C_{20}H_{25}N_3O_7$ requires: C, 57·27; H, 5·96; N, 10·02%).

2-(3,4,6-*Tri*-O-*acetyl*-2-*deoxy*-α-D-lyxo-*hexopyranosyl*)-5,6-*dimethylbenzotriazole* (VIf). The next moving band gave 0·5 g of VIf, m.p. 124–125° (from EtOH), $[\alpha]_D$ +82·2° (*c* 1, $CHCl_3$); λ_{max}^{EtOH}, 278 (ε, 10,300) (sh), 285 (ε, 12,000), 295 mμ (ε, 10,000). (Found: C, 57·18; H, 5·91; N, 10·12. $C_{20}H_{25}N_3O_7$ requires: C, 57·27; H, 5·96; N, 10·02%).

Reaction of 3,4,6-*tri*-O-*acetyl*-D-*galactal with* 5,6-*dichlorobenzotriazole*

The reaction was accomplished as for the preceding cases starting from 5·44 g (0·02 mole) of glycal and 1·88 g (0·01 mole) of 5,6-dichlorobenzotriazole. The crude product obtained after heating for 70 hr at 90–95° was dissolved in $CHCl_3$ and applied to 23 preparative TLC plates. The plates were developed 15 times in ether–light petroleum (3:4) resulting in the separation of 5 fractions.

1-(3,4,6-*Tri*-O-*acetyl*-2-*deoxy*-β-D-lyxo-*hexopyranosyl*)-5,6-*dichlorobenzotriazole* (Vc). The solid obtained from the slowest moving band (0·17 g) was recrystallized from EtOH–H_2O to give Vc, m.p. 160–161°, $[\alpha]_D$ −33·3° (*c* 1, $CHCl_3$): λ_{max}^{EtOH}, 262 (ε, 6480), 268 (ε, 6050) (sh), 296 (ε, 4300), 304 mμ (ε, 3360) (sh). (Found: C, 46·73; H, 4·20; N, 9·16. $C_{18}H_{19}Cl_2N_3O_7$ requires: C, 46·95; H, 4·13; N, 9·13%).

1-(3,4,6-*Tri*-O-*acetyl*-2-*deoxy*-α-D-lyxo-*hexopyranosyl*)-5,6-*dichlorobenzotriazole* (VIc). The next band gave 0·32 g of VIc, m.p. 151·5–152° (from EtOH–H_2O), $[\alpha]_D$ +198·9 (*c* 1, $CHCl_3$); λ_{max}^{EtOH}, 263 (ε, 6900), 270 (ε, 6570) (sh), 296 (ε, 4500), 304 mμ (ε, 3560) (sh). (Found: C, 47·04; H, 4·32; N, 9·22. $C_{18}H_{19}Cl_2N_3O_7$ requires: C, 46·95; H, 4·13; N, 9·13%).

1-(4,6-*Di*-O-*acetyl*-2,3-*dideoxy*-α-D-threo-*hex*-2-*enopyranosyl*)-5,6-*dichlorobenzotriazole* (VIIc). The solid obtained from the following band was recrystallized from EtOH to yield 0·04 g of VIIc, m.p. 196°, $[\alpha]_D^{30°}$ +24·6° (*c* 0·25, EtOH): λ_{max}^{EtOH}, 262 (ε, 8950), 268 (ε, 9000), 292 (ε, 9650), 301 mμ (ε, 7180) (sh). (Found: C, 48·05; H, 3·82; N, 10·79. $C_{16}H_{15}Cl_2N_3O_5$ requires: C, 48·00; H, 3·75; N, 10·50%).

2-(3,4,6-*Tri*-O-*acetyl*-2-*deoxy*-α-D-lyxo-*hexopyranosyl*)-5,6-*dichlorobenzotriazole* (VIg). The fourth band gave 0·6 g of VIg, m.p. 117–118° (from EtOH), $[\alpha]_D$ +86·0° (*c* 1, $CHCl_3$); λ_{max}^{EtOH}, 287 (ε, 11,500) (sh), 296 (ε, 13,700), 305 mμ (ε, 12,350). (Found: C, 47·11; H, 4·19; N, 8·87. $C_{18}H_{19}Cl_2N_3O_7$ requires: C, 46·95; H, 4·13; N, 9·13%). Finally, from the fastest moving band 5,6-dichlorobenzotriazole was isolated.

Reaction of 3,4,6-*tri*-O-*acetyl*-D-*galactal with* 6-*chloropurine*

A mixture of glycal (5·44 g, 0·02 mole) and 6-chloropurine (1·55 g, 0·01 mole) was heated for 44 hr as in the preceding cases. After this time a small amount (0·35 g) of a solid was removed by filtration and the solution was washed with water, and finally dried over Na_2SO_4. The crude thick syrup obtained after removing the solvent was dissolved in $CHCl_3$ and chromatographed on 20 preparative TLC plates using ether resulting in the separation of two major bands.

The slow band gave unreacted 6-chloropurine while rechromatography of the material obtained from the fast band (2·3 g) using ether–light petroleum (5:1) gave two fractions.

6-*Chloro*-9-(3,4,6-*tri*-O-*acetyl*-2-*deoxy*-β-D-lyxo-*hexopyranosyl*)*purine* (Vd). The slow band afforded 0·53 g of Vd, m.p. 145–146° (from EtOAc–light petroleum), $[\alpha]_D$ +2° (*c* 0·7, $CHCl_3$); λ_{max}^{EtOH}, 264 mμ (ε, 9170). (Found: C, 47·55; H, 4·59; N, 13·02; Cl, 8·33. $C_{17}H_{19}ClN_4O_7$ requires: C, 47·84; H, 4·45; N, 13·13; Cl, 8·30%).

6-*Chloro*-9-(3,4,6-*tri*-O-*acetyl*-2-*deoxy*-α-D-lyxo-*hexopyranosyl*)*purine* (VId). The fast moving band gave 0·65 g of a syrup which was rechromatographed (EtOAc–$CHCl_3$, 1:1) to give pure VId, $[\alpha]_D$ +58·0° (*c* 0·7, $CHCl_3$): λ_{max}^{EtOH}, 264 mμ (ε, 9120). (Found: C, 47·59; H, 4·48; N, 13·18. $C_{17}H_{19}ClN_4O_7$ requires: C, 47·84; H, 4·45, N, 13·13%).

Acknowledgments—The authors express their gratitude to Professor M. Lora-Tamayo for his constant encouragement. This work was supported by a grant from the Fondo Nacional para el Fomento de la Investigación.

REFERENCES

[1] R. K. Robins, E. F. Godefroi, E. C. Taylor, L. R. Lewis and A. Jackson, *J. Am. Chem. Soc.* **83**, 2574 (1961)

[2] [a] E. E. Leutzinger, W. A. Bowles, R. K. Robins and L. B. Townsend, *Ibid.* **90**, 127 (1968); [b] E. E. Leutzinger, R. K. Robins and L. B. Townsend, *Tetrahedron Letters* 3751 (1970); [c] N. Nagasawa, I. Kumashiro and T. Takenishi, *J. Org. Chem.* **32**, 251 (1967); [d] K. Onodera and T. Yajima, *Carbohyd. Res.* **13**, 97 (1970); [e] M. Fuertes, G. García-Muñoz, R. Madroñero, M. Stud and M. Rico, *Tetrahedron* **26**, 4823 (1970); [f] *Ibid.* **28**, 623 (1972); [g] R. J. Ferrier and M. M. Ponpipom, *J. Chem. Soc.* (C) 553–560 (1971)

[3] R. H. Wiley, N. R. Smith, D. M. Johnson and J. Moffat, *J. Am. Chem. Soc.* **76**, 4933 (1954)

[4] C. W. Schellhamer, J. Schoeder and N. Joop, *Tetrahedron* **26**, 497 (1970)

[5] R. H. Wiley and K. F. Hussung, *J. Am. Chem. Soc.* **79**, 4395 (1957)

[6] R. J. Abraham, H. Gottschalk, H. Paulsen and W. A. Thomas, *J. Chem. Soc.* 6269 (1965)

[7] E. W. Garbisch, *J. Am. Chem. Soc.* **86**, 5561 (1964)
[8] R. U. Lemieux, E. Fraga and K. A. Watanabe, *Canad. J. Chem.* **46**, 61 (1968)
[9] K. Bock, I. Lund and C. Pedersen, *Acta Chem. Scand.* **23**, 2083 (1969); L. D. Hall and J. F. Manville, *Adv. Chem. Series* **74**, 228 (1968)