Tetrahedron. Vol. 26, pp. 4823 to 4837 Pergamon Press 1970. Printed in Great Britain

HETEROCYCLIC N-GLYCOSIDES—V

SYNTHESIS OF UNSATURATED N-GLYCOSIDES FROM 6-CHLOROPURINE AND DERIVATIVES OF D-XYLAL AND L-ARABINAL. A CONFORMATIONAL NMR STUDY

M. FUERTES, G. GARCIA-MUÑOZ, 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* 13 *May* 1970; *Accepted for publication* 15 *June* 1970)

Abstract—The acid-catalyzed reaction of 6-chloropurine with 3,4-di-O-acetyl-D-xylal yielded four compounds. The main products were shown to be the corresponding 6-chloro-9-(4′-O-acetyl-2′,3′-dideoxy-α and β-D-*glycero*-pent-2′-enosyl)purine, and 1,2,3-trideoxy-4-O-acetyl-3-(6′-chloro-9′-purinyl) D-*threo*-pent-1-enopyranose. On the other hand reaction of 6-chloropurine with 3,4-di-O-acetyl-L-arabinal yielded, in addition to the enantiomers of the above compounds, 6-chloro-9-(3′,4′-di-O-acetyl-2′-deoxy-α- and β-L-*erythro*-pentopyranosyl)purine. A NMR study of these compounds showed that the previous reported assignations for 6-chloro-9-(3′,4′-di-O-acetyl-2′-deoxy-α- and β-D-*erythro*-pentopyranosyl) purine are in error. The conformations of all compounds obtained, as determined from their NMR parameters, are discussed.

PREVIOUS work[1] on the synthesis of 2′,3′-unsaturated heterocyclic N-glycosides by reaction of benzotriazoles and glycals in ethyl acetate solution and in the presence of a catalytic amount of trifluoroacetic acid has proved to be of interest for the preparation of such compounds. These substances can be of value in biological studies and as intermediates in the preparation of other N-glycosides.

The possibility of using glycals in nucleoside synthesis was first suggested by Robins[2] in a study on the reaction of several purines and 2,3-dihydrofuran and dihydro-4*H*-pyran. More recently,[3] the same author has described the preparation of certain 9-(2′-deoxy-*erythro*-pentopyranosyl) purines by addition of 6-chloropurine and 2,6-dichloropurine to the double bond of 3,4-di-O-acetyl-D-arabinal in a procedure involving the fusion of the purine and the glycal in the presence of sulfanilic acid.

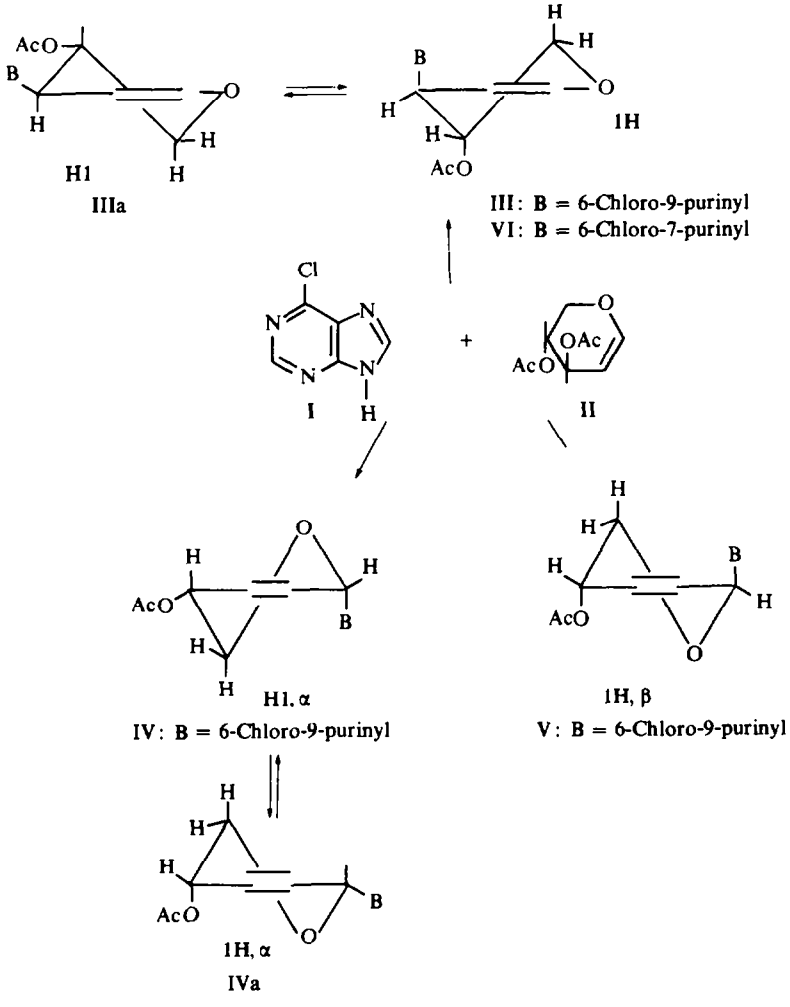
Since the results of our work with benzotriazoles differed from those described by Robins *et al.*[3] with respect to the nature of the N-glycosides obtained, we decided to study the reaction of 6-chloropurine with 3,4-di-O-acetyl-D-xylal and 3,4-di-O-acetyl-L-arabinal under the experimental conditions used in our initial studies,[1] i.e. the reaction of these same glycals with benzotriazole and 5,6-dimethylbenzotriazole.

When a mixture of 6-chloropurine (I) and 3,4-di-O-acetyl-D-xylal (II) in ethyl acetate containing a few drops of trifluoracetic acid was heated in a sealed tube at

95° under continuous agitation for 24 hr, four compounds were obtained, which were separated by thick-layer chromatography: 1,2,3-trideoxy-4-O-acetyl-3-(6'-chloro-9'-purinyl) D-*threo*-pent-1-enopyranose (III), 6-chloro-9-(4'-O-acetyl-2',3'-dideoxy-α-D-*glycero*-pent-2'-enosyl)purine (IV), 6- chloro-9-(4'-O-acetyl-2',3'- dideoxy-β-D-*glycero*-pent-2'-enosyl) purine (V), and 1,2,3-trideoxy-4-O-acetyl-3-(6'-chloro-7'-purinyl) D-*threo*-pent-1-enopyranose (VI).

Mass spectrometry showed the four compounds to have the same molecular mass. Furthermore, the identity of the mass spectra of IV and V suggested that these products are a pair of configurational isomers.

The site of glycosidation was ascertained to be N-9 for compounds III, IV and V



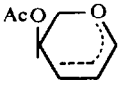
and N-7 for compound VI by a comparison (Table 1) of their UV spectra with the UV spectra of 6-chloro-7-methylpurine and 6-chloro-9-methylpurine.[2]

PMR parameters obtained for compounds III and VI are given in Table 2. The NMR spectrum of III in deuteriochloroform is complicated by the strong coupling

between the H-3 and H-4 protons which causes the appearance of second-order effects in the multiplets arising from the remaining protons in the system. A complete analysis of this spectrum was made using the NMRIT and NMREN programs. Some 70 lines were measured and assigned; the mean deviation between observed and calculated line frequencies was 0·17 Hz. The maximum errors in the parameters were ±0·01 ppm for the chemical shifts, and ±0·1 Hz for the coupling constants. The NMR spectra of this compound in hexadeuteriobenzene and that of VI in deuteriochloroform were interpreted by a first order analysis. The errors in the parameters for the latter spectra were ±0·01 ppm for the chemical shifts, and ±0·2 Hz for the coupling constants.

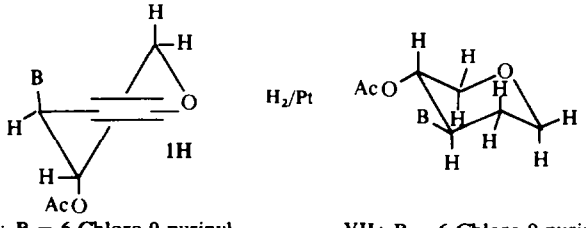
The very similar values for the coupling constants of III and VI strongly suggested that both compounds have the same configuration and conformation. Hence, in the following discussion we will refer to III alone, and the conclusions drawn may be applied to VI as well.

IR absorptions at 1646, and 1228 cm^{-1} in III suggested a α,β-unsaturated ether, and NMR support for this feature was provided by two signals at τ 3·15 and τ 5·02, ascribable to the olefinic protons, with a coupling constant $J_{1,2}$ of 6·0 Hz, excellent proof of a glycal.[4] On the other hand, in view of the recently reported statement,[5] that in the reaction with which we are concerned the carbonium ion (X) would be the reacting species, there can be little doubt that the 6-chloropurine moiety in III must be bonded to C-3 in the sugar.



X

Catalytic hydrogenation of III gave a syrupy compound VII. PMR parameters for this compound are given in Table 3. The multiplets at τ 5·28 and τ 4·55 were assigned to the H-3 and H-4 protons, respectively. The high value for the coupling constant $J_{3,4}$ (10·4 Hz) requires the axial orientation for both H-3 and H-4.



III: B = 6-Chloro-9-purinyl VII: B = 6-Chloro-9-purinyl

After the structure and configuration of compound III had been established, the conformation of the dihydropyran ring still remained to be determined. In the discussion of this subject we shall refer only to the two half-chair conformations H1 and 1H, which are considered to be the ones with the lowest energy.[6]

The values to be expected for coupling constants $J_{3,4}$, $J_{4,5e}$ and $J_{4,5a}$ in the case of an 1H form (III) are about 2·2 Hz[7] or even lower,[8] and $J_{2,3}$ should be about 5·7 Hz.[7,8] On the other hand, the values to be expected for $J_{4,5a}$ and $J_{4,5e}$ for an H1

conformation (IIIa) are approximately 9·5 and 4·5 Hz respectively.[8,9] In turn, the value of $J_{2,3}$ should be 2 Hz, and $J_{3,4}$ should be about 7·5 Hz.[9] In the case of the 3,4,6-tri-O-acetyl-D-glucal the values reported[10] for $J_{2,3}$, $J_{3,4}$, and $J_{4,5a}$ are 3·2, 6·4 and 6·8 Hz respectively; these data show that this compound is preferentially in the H1 conformation.

A comparison of the values obtained for the coupling constants between neighbouring proton in III (Table 2) with the above figures reveals that the former are in close agreement with those of a 1H conformation, although they all lie in the range intermediate between the values expected for each of the two half-chair conformations.*

Moreover, the remarkably high values for the long-range coupling constants $^4J_{2,4}$ and $^4J_{3,5e}$ (Table 2) also support the view that the sugar in compound III is preferentially in the 1H conformation. Such a conformation places the proton involved in the above couplings in the zig-zag or W configuration which has been shown to be the one most suited for long-range couplings of that magnitude.

In order to obtain additional evidence in favour of the foregoing assignments, we studied the NMR spectra of di-O-acetyl-D-xylal and di-O-acetyl-L-arabinal. Table 4 lists the magnetic parameters obtained from the NMR spectra of these two compounds. In the case of di-O-acetyl-L-arabinal (benzene-d_6, 60 M Hz), the accidental degeneracy of H-5a and H-5e allows the determination of only the value for the sum of the coupling constants between these protons and others. The value for the sum $(J_{4,5a} + J_{4,5e})$ (12·9 Hz) implies a large value for $J_{4,5a}$, which establishes that H-4 is axially oriented. The value for the sum $(J_{3,5a} + J_{3,5e})$ (1·6 Hz) indicates in turn that there is a large long-range coupling constant, which must obviously be $J_{3,5e}$. The values for these coupling constants, together with the remaining ones contained in Table 5, are in general agreement with the ones to be expected for a 1H(L) conformation.†

The NMR spectrum of di-O-acetyl-D-xylal is complicated by the near coincidence of the resonances of H2, H3 and H4. Nevertheless, the magnetic parameters that could be obtained (benzene-d_6, 60 MHz) were very similar to the ones for III (Table 2). This agreement suggests that di-O-acetyl-D-xylal and III have the same configurations (C-3 and C-4), and that they reside in the same 1H conformations. Ferrier,[7] in a study on 2,3,4-tri-O-acetyl-2-hydroxy-D-xylal, reached the conclusion that this compound also is in this conformation, and attributed this fact to the absence of the CH_2OAc group on C-5, unlike 2,3,4,6-tetra-O-acetyl-2-hydroxy-D-glucal, which is in the H1 conformation.

The fact that the values obtained for the coupling constants in III are intermediate between the ones that might be expected for the two half-chair conformations suggest that III is not conformationally homogeneous, and that its NMR spectrum reflects an average of the two conformations in rapid interconversion. Horton[11] and Bhacca[12]

* Only the allylic constant $^4J_{1,3}$ had a value differing from the expected one. This constant is −0·8 Hz for 3,4-di-O-acetylarabinal, (Table 4), and −1·3 Hz for 3,4,6-tri-O-acetylglucal[10]; the values for $^4J_{1,3}$ in III and VI might have been expected to lie within these limits. However, we believe that the observed differences between the experimental values for III and VI and the values for the above mentioned glycals may be attributed primarily to the substitution of the 6-chloropurine for the acetoxy group.

† In this paper, H1 and 1H invariably refer to D-sugars while H1 (L) and 1H(L) refer to L-sugars. It must be kept in mind that the H1 form of the D-series and the 1H(L) form of the L-series are mirror images and that the substituents in each case will therefore have the same axial or equatorial arrangement.

have recently shown by low-temperature NMR studies that a conformational equilibrium exists between the 1C and C1 chair forms in a series of D-aldopentopyranose tetra-acetates. A similar equilibrium between the 1H and H1 forms is possible in our compounds, since the activation free energy for this equilibrium in dihydropyran (6·6 Kcal/mol)[6] is less than the corresponding one for the interconversion equilibrium between 1C and C1 forms in tetrahydropyran (10·5 Kcal/mol).[13]

The differences observed in the values for the coupling constants in III in deuteriochloroform and benzene-d_6 also suggests the existence of a conformational equilibrium. The interaction between the electrical dipoles C-3-base and C-4-OAc is stronger in benzene, a solvent with a lower dielectric constant than chloroform; thus, it is to be expected that the 1H form population will be greater in the former than in the latter.

Compounds IV and V, which are a pair of anomers, show very similar NMR spectra. A complete iterative analysis of both spectra was performed using the NMRIT and NMREN programs. A total of about fifty lines was measured for each compound, and the mean deviation between observed and calculated line frequencies in each case was ±0·10 Hz. The maximum errors were ±0·01 ppm for the chemical shifts and ±0·05 Hz for the coupling constants. The magnetic parameters obtained (100 MHz, deuteriochloroform) are shown in Table 5.

In the case of compound V, the value for the sum ($J_{4',5'a} + J_{4',5'e}$) (5·76 Hz) is close to that expected for 2,3-unsaturated pentopyranosyl derivatives in the 1H form (4 Hz),[14] and far from the value for the H1 form (about 14 Hz). Likewise, the value for $J_{3',4'}$ (4·53 Hz), while intermediate between the values predictable for 1H and H1 half-chair conformations (approximately 5·7 and 2·0 Hz respectively)[9,15] is nevertheless closer to the value for the 1H form. The values for $J_{1,2}$ in analogous molecules where the substituent on the anomeric carbon is an acetoxyl group lie between 2·0 and 2·6 Hz (when the anomeric proton is pseudoequatorial) and between 0·8 and 1·3 Hz (when this proton is pseudoaxial). The value we found, for $J_{1',2'}$ (3·13 Hz) suggests that the anomeric proton in V occupies a pseudoequatorial position. The value obtained for the homoallylic coupling constant $^5J_{1',4'}$ (0·82 Hz) is likewise compatible with a pseudoequatorial-pseudoequatorial relative arrangement of protons H-1′ and H-4′.[16] Nevertheless, this value is higher than the one reported by Lemieux *et al.*[8] ($^5J_{1,4} < 0·3$ Hz) for methyl 4,6-O-benzylidene-α-D-*threo*-hex-2-enopyranoside.

In view of the foregoing results, it seems that compound V 6-chloro-9-(4′-O-acetyl-2′,3′-dideoxy-β-D-*glycero*-pent-2′-enosyl) purine resides primarily in the 1H conformation as shown in the figure. It should be pointed out that in the literature[7] are described several 2,3-didehydro-3-deoxyaldose derivatives in which the β anomer invariably exists in the 1H half-chair conformation.

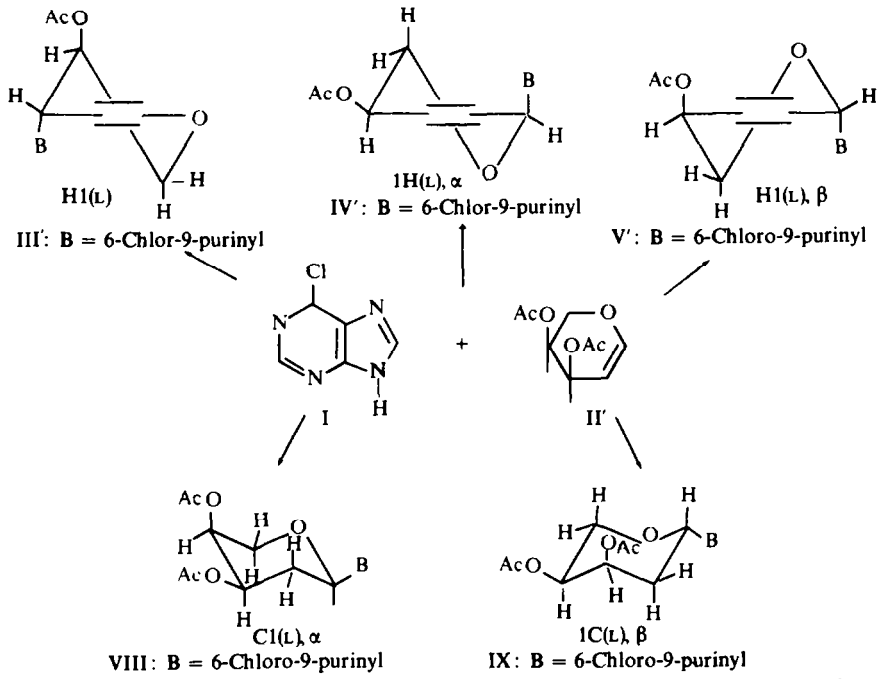
To account for the somewhat large value of $^5J_{1,4}$, the existence of a small proportion of the H1 form in conformational equilibrium with the more abundant 1H form is not discarded.

As for compound IV, the assignment of configuration to the anomeric carbon is based on the fact that, no matter whether the conformation is 1H or H1, there will always be a pseudoaxial-pseudoequatorial relationship between protons H-1′ and H-4′, in which case a value of about 1·3–1·7 Hz may be expected for $^5J_{1',4'}$.[8,14,16] The value we obtained for this coupling constant (1·90 Hz) is more compatible with

the postulated stereochemical arrangement than with any other possible one.* The conformation of this compound could not be immediately deduced, for the values for constant $J_{3',4'}$ (3·52 Hz) and for sum ($J_{4'5'a} + J_{4',5'e}$) (9·46 Hz) were intermediate between the ones predictable for the two conformations, 1H and H1 ($J_{3',4'} = 5{\cdot}7$ Hz and ($J_{4',5'a} + J_{4',5'e}$) = 4 Hz for 1H form, and $J_{3',4'} = 2{\cdot}0$ Hz and ($J_{4',5'a} + J_{4',5'e}$) = 14 Hz for H1 form).

It is thus clear that the coupling constants found for IV, while intermediate between the values mentioned above, are closer to the ones for an H1 form. This discrepancy between the experimental values and the predicted ones for both conformations can be explained on the hypothesis that the energy barrier separating the two forms is low, and the interconversion between them is therefore fast enough for the magnetic parameters observed at room temperature to be characteristic of an averaged NMR spectrum. Consequently, we assume compound IV [6-chloro-9-(4'-O-acetyl-2',3'-dideoxy-α-D-*glycero*-pent-2'-enosyl) purine] to be a mixture in equilibrium of the two conformers, IV and IVa in which the H1 conformer (IV) predominates slightly.

When 6-chloropurine was reacted with di-O-acetyl-L-arabinal, the optical antipodes III', IV' and V' of compounds III, IV and V were obtained. Together with these derivates, two N-glycosides were also obtained, one with m.p. 149–150°, $[\alpha]_D$ = +33·5 (*c* 0·7, ethyl acetate) (VIII), and the other with m.p. 203–205°, $[\alpha]_D$ −21·3 (*c* 0·8, acetone) (IX), which are the optical antipodes of the ones obtained by Leutzinger *et al.*[3] by reacting 6-chloropurine with di-O-acetal-D-arabinal. The products were shown by these authors to be the corresponding 6-chloro-9-(3',4'-di-O-acetyl-2'-deoxy-α-D-*erythro*-pentopyranosyl)purine, m.p. 205–207°, $[\alpha]_D^{26}$ +21·8° (*c* 0·75,



* This coupling constant would be around 3 Hz for a pseudoaxial-pseudoaxial arrangement, and around 1 Hz for an pseudoequatorial-pseudoequatorial arrangement.[8,16]

acetone), and 6-chloro-9-(3′,4′-di-O-acetyl-2′-deoxy-β-D-*erythro*-pentopyranosyl)-purine, m.p. 149–150° $[\alpha]_D^{26}$ −33·6° (*c* 1·0, ethyl acetate), respectively, and it was proved beyond doubt that these anomers existed in different conformations.

A study of the NMR spectra of VIII and IX led us to reverse the assigned conformations as made by the above-mentioned authors. Thus, as we will show below, the compound with m.p. 205–207° is the β-anomer (IX), while the one with m.p. 149–150° is the α-anomer (VIII).

Table 6 contains the magnetic parameters we obtained from the NMR spectra for VIII and IX. The above mentioned authors devote their attention primarily to the spectrum of the anomer with m.p. 205–207°. The values for $J_{2'a,3'}$ (6·9 Hz) and $J_{2'e,3'}$ (0 Hz) that they obtain from the quartet at δ 5·65 (4·32 τ, according to our measurements) and assign to H-3′, do not account for this multiplet, whose bands stand in an approximate intensity ratio of 1:3:3:1. The above quoted values for the coupling constants can only be considered correct if the resonance of H-2′a and H-2′e are accidentally degenerate. This is not the case; in the H-1′ quartet, for example, the individual couplings of this proton with H-2′ and H-2′e are observable; and the same authors, in a double resonance experiment, observed H-1′ to be a doublet ($J_{1',2'e}$ 3·7 Hz) when H-2′a was decoupled.

The values we obtained by first-order analysis of the quartet at δ 5·65 (4·32 τ in our case) for the coupling constants of the H-3′ proton with H-2′a, H-2′e, and H-4′ were $J_{2'a,3'} = 3{\cdot}4$ Hz, $J_{2'e,3'} = 3{\cdot}4$ Hz and $J_{3',4'} = 3{\cdot}1$ Hz, which are fully compatible with an equatorial arrangement of proton H-3′, and not with an axial one.

Protons H-5′a and H-5′e, whose chemical shifts accidentally coincide, give rise to a doublet centered at 5·94 τ with a separation of 8 Hz (7·7 Hz in our case) due to coupling to H-4′. In such a situation the value for the splitting observed is equal to the half-sum $\frac{1}{2}(J_{4',5'a} + J_{4',5'e})$; hence, the value of the sum $(J_{4',5'a} + J_{4',5'e})$ must be 15·4 Hz. Thus, the values obtained by the above mentioned authors for $J_{4',5'a}$ (8·0 Hz) and $J_{4',5'e}$ (−0·1 Hz) are incorrect. Since the value of this sum is high enough to include a coupling constant of the axial–axial type (~10 Hz), H-4′ must be assigned an axial position.

The preceding conclusions, together with those of Leutzinger *et al.*, i.e., that the above mentioned compounds are a pair of anomers and that the anomeric proton is axial in both of them, make it possible to assign a β configuration to the compound with m.p. 203–205°. In this compound (IX), the carbohydrate moiety adopts the C1 conformation when obtained from D-arabinal and the 1C(L) conformation when obtained from L-arabinal.

The NMR spectrum of the product (VIII) with m.p. 149–150° in turn yielded independent information enabling it to be assigned a α configuration with the carbohydrate moiety in the C1 (L) conformation when obtained from L-arabinal. The H-5′a and H-5′e part of the spectrum could be analyzed as the AB part of an ABX system. The values for the coupling constants ($J_{4',5'a} = 1{\cdot}7$ Hz, $J_{4',5'e} = 2{\cdot}4$ Hz and $J_{5'a,5'e} = -13{\cdot}5$ Hz) obtained from this analysis indicated that the H-4′ proton is equatorially oriented and this fact, together with the previously obtained information on the anomeric proton, is sufficient for the determination of the sugar conformation.

The differences observed in the reactivities of the two glycals used (absence of saturated nucleosides in the case of the reaction with di-O-acetyl-D-xylal) can be explained on the ground that the acetoxy group on C-4 in the D-xylal facilitates

elimination of the acetoxy group on C-3. Similar results have been described by Ferrier[5,17] in studies with D-glucal and D-galactal derivatives, and by Pedersen[18] in work on the reaction of di-O-acetyl-D-xylal and di-O-acetyl-D-arabinal with hydrogen halides.

TABLE 1. ULTRAVIOLET ABSORPTION SPECTRA OF THE PRODUCTS OBTAINED AND RELATED 9- AND 7-METHYLPURINES

Compound	λ_{max}^{EtOH}	ε	pH 11		pH 1	
			λ_{max}	ε	λ_{max}	ε
III	265	9,250	265	9,000	265	9,225
IV	264	9,920	263	9,350	264	9,800
V	265	9,920	262	8,990	264·5	9,765
VI	272	6,689	262	7,070	272	6,580
6-chloro-9-methylpurine[2]	265	9,100				
6-chloro-7-methylpurine[2]	271	7,300				

EXPERIMENTAL

M.ps are uncorrected. IR spectra were taken on a Perkin–Elmer 137 spectrophotometer. UV absorption spectra were recorded on a Perkin–Elmer 350 spectrophotometer. The NMR spectra were obtained with Perkin–Elmer R-10 and Varian HA-100 spectrometers using TMS as the internal standard. Optical rotations were determined on a Perkin–Elmer 141 polarimeter. Mass spectra were obtained with AEI MS9 and AEI MS12 instruments.

Reaction of 6-chloropurine and 3,4-di-O-acetyl-D-xylal. A mixture of 1·55 g (0·01 mole) 6-chloropurine 4 g (0·02 mole) 3,4-di-O-acetyl-D-xylal[19] in 70 ml pure EtOAc with a few drops trifluoroacetic acid catalyst was heated in sealed tube under continuous agitation at 95° for 24 hr. After this time a small amount (~0·1 g) of a solid was removed by filtration and the soln was washed with water, and finally dried over Na_2SO_4. The EtOAc was evaporated under reduced press to a thick syrup, which was left overnight *in vacuo* over P_2O_5 and KOH.

This syrup (4·33 g) was dissolved in $CHCl_3$ and applied to 15 preparative TLC plates (20 × 20 cm, and 2 mm thickness silica gel, Merck PF_{254}). The plate were developed in a mixture of ether–light petroleum (2:1) allowing the solvent to run the total length of the plates and dried. This procedure was repeated 10 times resulting in the separation of the 4 major components which were detected by a UV lamp (254 mμ). In all the cases products were extracted with EtOAc.

1,2,3-*Trideoxy*-4-O-*acetyl*-3-(6′-*chloro*-9′-*purinyl*) D-threo-*pent*-1-*enopyranose* (III). The faster moving band gave 0·1 g of a white solid, m.p. 136–137° (from AcOEt–light petroleum), $[\alpha]_D$ −84·3° (*c* 0·43 $CHCl_3$). (Found: C, 49·17; H, 3·79; N, 18·93; M^+ 294; 296. $C_{12}H_{11}ClN_4O_3$ requires: C, 48·89; H, 3·73; N, 19·01%; M.W. 294; 296).

6-*Chloro*-9-(4′-O-*acetyl*-2′,3′-*dideoxy*-α-D-glycero-*pent*-2′-*enosyl*) *purine* (IV). The following band gave 0·5 g of a syrup which was rechromatographed to a pure material, $[\alpha]_D$ −73·3° (*c* ~ 1·0, $CHCl_3$). (Found: M^+ 294; 296. $C_{12}H_{11}ClN_4O_3$ requires: M.W. 294; 296).

6-*Chloro*-9-(4′-O-*acetyl*-2′,3′-*dideoxy*-β-D-glycero-*pent*-2′-*enosyl*) *purine* (V). The next band gave 1·06 g of a white solid, m.p. 101–102° (from MeOH); $[\alpha]_D$ +152·1° (*c* 1·1, $CHCl_3$). (Found: C, 47·49; H, 3·55; N, 18·44: M^+ 294; 296. $C_{12}H_{11}ClN_4O_3 \cdot \frac{1}{2}H_2O$ requires: C, 47·47; N, 3·95; N, 18·45%; M.W. 294; 296).

1,2,3-*Trideoxy*-4-O-*acetyl*-3-(6′-*chloro*-7′-*purinyl*) D-threo-*pent*-1-*enopyranose* (VI). The slower moving band gave 0·14 g of a solid which was shown to be a mixture of 6-chloropurine and VI. These two compounds were separated by thick-layer chromatography (silica gel PF_{254}, Merck). The plates were developed several times in a mixture of ether–light petroleum (2:1). The slower moving band was removed and extracted with EtOAc. The soln obtained was concentrated *in vacuo* to a solid, m.p. 134–136° (EtOAc-light petroleum); $[\alpha]_D$ +88·6° (*c* 0·9, $CHCl_3$). (Found: C, 48·81; H, 3·73; N, 19·27; Cl, 12·27, $C_{12}H_{11}ClN_4O_3$ requires: C, 48·91; H, 3·73; N, 19·02; Cl, 12·02%).

TABLE 2. NMR SPECTRAL PARAMETERS OF 1,2,3-TRIDEOXY-4-O-ACETYL-3-(6 '-CHLORO-9 '-PURINYL)-D-*threo*-PENT-1-ENOPYRANOSE (III) AND 1,2,3-TRIDEOXY-4-O-ACETYL-3-(6 '-CHLORO-7 '-PURINYL)-D-*threo*-PENT-1-ENOPYRANOSE (VI)

Chemical Shifts (τ-values)

Comp.	Solv.	ν_0(MHz)	H-1	H-2	H-3	H-4	H-5a	H-5e[a]	H'-2 and H'-8	AcO
III	CCl_3D	100	3·15	5·02	4·70	4·74	5·96	5·82	1·24 ---------1·70	7·84
III	Benzene-d_6	60	3·66	5·78	4·99	5·23	6·65	6·17	1·41 ---------2·39	8·47
VI	CCl_3D	60	3·06	4·96	4·49	4·75	6·09	5·77	1·16 ---------1·49	7·91

Coupling constants (Hz)

			$J_{1,2}$	$J_{1,3}$[b]	$J_{2,3}$	$J_{2,4}$	$J_{3,4}$	$J_{3,5e}$	$J_{4,5a}$	$J_{4,5e}$	$J_{5a,5e}$[b]
III	CCl_3D	100	6·0	−1·0	3·9	1·0	4·0	1·5	2·7	4·8	−12·0
III	Benzene-d_6	60	6·1	−1·4	4·4	1·4	3·8	1·7	2·2	4·3	−12·4
VI	CCl_3D	60	6·0	−1·8	4·7	1·6	?	1·5	2·4	4·2	−12·4

[a] H-5e was assigned to the signal that showed a long-range coupling of ~1·5 Hz.

[b] Signs assumed negative.

TABLE 3. NMR SPECTRAL PARAMETERS OF VII (Cl_3CD, 60 MHz)

Chemical Shifts (τ-values)

H-1a	H-1e	H-3a	H-4a	H-5a	H-5e	H-2a		H-2e	H-2′ and H-8′		AcO
6·43	5·86	5·28	4·55	6·67	5·77	7	to	8	1·29	1·80	8·25

Coupling constants (Hz)

$J_{2a,3a}$	$J_{2e,3a}$	$J_{3a,4a}$	$J_{4a,5a}$	$J_{4a,5e}$	$J_{5a,5e}$[a]
11·2	4·9	10·4	10·0	5·1	−11·0

[a] Sign assumed negative.

TABLE 4. NMR SPECTRA PARAMETERS OF DI-O-ACETYL-L-ARABINAL AND DI-O-ACETYL-D-XYLAL

Chemical Shifts (τ-values)

Comp.	Solv.	ν_0(MHz)	H-1	H-2	H-3	H-4	H-5a	H-5e	AcO	
Arab.	CCl_3D	60	3·52	4·87	4·57	6·04	6·04		7·91	7·97
Arab.	Benzene-d_6	60	3·61	4·82	4·50	6·09	6·09		8·14	8·14
Xylal	CCl_3D	60	3·42	5·06	5·06	6·05	6·05	5·82	7·91	7·95
Xylal	Benzene-d_6	60	3·51	5·04	5·04	6·16	6·16	5·94	8·20	8·20

Coupling Constants (Hz)

			$J_{1,2}$	$J_{1,3}$[a]	$J_{2,3}$	$J_{2,4}$	$J_{3,4}$	$J_{3,5e}$	$J_{4,5a}$	$J_{4,5e}$	$J_{5a,5e}$[a]
Arab.	Benzene-d_6	60	6·1	−0·8	5·0	0·0	3·7	1·6	sum	12·9	?
Xylal	Benzene-d_6	60	?	?	4·2	1·5	?	1·5	1·8	3·3	−12·4

[a] Signs assumed negative.

TABLE 5. NMR SPECTRAL PARAMETERS OF 6-CHLORO-9-(4'-O-ACETYL-2',3'-DIDEOXY-α-D-*glycero*-PENT-2'-ENOSYL) PURINE (IV) AND 6-CHLORO-9-(4'-O-ACETYL-2',3'-DIDEOXY-β-D-GLYCERO-PENT-2'-ENOSYL) PURINE (V)

Chemical Shifts (τ-values)

Comp.	Solv.	ν_0(Hz)	H-1'	H-2'	H-3'	H-4'	H-5'a	H-5'e	H-2 and H-8		AcO
IV	CCl_3D	100	3·42	3·78	3·54	4·65	6·13	5·90	1·20	1·66	7·87
V	CCl_3D	100	3·37	3·67	3·46	4·74	5·99		1·20	1·76	7·88

Coupling Constants (Hz)

			$J_{1',2'}$	$J_{1',3'}$[a]	$J_{1',4'}$	$J_{2',3'}$	$J_{2',4'}$[a]	$J_{3',4'}$	$J_{4',5'a}$		$J_{4',5'e}$	$J_{5'a,5'e}$[a]
IV	CCl_3D	100	2·03	−2·03	1·90	10·00	−1·24	3·52	5·21		4·25	−12·20
V	CCl_3D	100	3·13	−1·83	0·82	10·08	−1·13	4·53		sum 5·76		?

[a] Signs assumed negative.

TABLE 6. NMR SPECTRAL PARAMETERS OF 6-CHLORO-9-(3',4'-DI-O-ACETYL-2'-DEOXY-α-L-*erythro*-PENTOPYRANOSYL)PURINE (VIII) AND 6-CHLORO-9-(3',4'-DI-O-ACETYL-2'-DEOXY-β-L-*erythro*-PENTOPYRANOSYL)PURINE (IX) (Cl_3CD, 60 MHz)

Chemical shifts (τ-values)

Comp.	Anomer	H-1'	H-2'a	H-2'e	H-3'	H-4'	H-5'a	H-5'e[a]	H-2 and H-8	AcO	
VIII	α	4·00	7·36*	7·57*		4·70	6·01	5·74	1·62, 1·27	7·80	7·94
IX	β	3·82	7·30*	7·50*	4·32	4·82	5·94		1·68, 1·25	7·80	7·94

Coupling constants (Hz)

	m.p.	$J_{1',2'a}$	$J_{1',2'e}$	$J_{2'a,2'e}$	$J_{2'a,3'}$	$J_{2'e,3'}$	$J_{3',4'}$	$J_{4',5'a}$	$J_{4',5'e}$	$J_{5'a,5'e}$
VIII	149–150°	10·0	3·6	−12·9*	11·6*	5·1*	?	1·7	2·4	−13·5
IX	203–205°	9·0	3·9	?	3·4	3·4	3·1	sum 15·4		?

[a] Low-field signal was assigned to H-5'e.

* Marked values are tentative.

Reaction of 6-chloropurine and 3,4-di-O-acetyl-L-arabinal. Under the same conditions used in the preceding case, 6-chloropurine (0·01 mole) and 3,4-di-O-acetyl-L-arabinal[20] (0·02 mole) furnished 4·6 g of a thick syrup. This material was chromatographed as before resulting in the separation of the following five compounds.

1,2,3-*Trideoxy*-4-O-*acetyl*-3-(6'-*chloro*-9'-*purinyl*) L-threo-*pent*-1-*enopyranose* (III'). The faster moving band gave 0·11 g of a solid. One recrystallization from EtOAc–light petroleum afforded pure III' m.p. 137·5–138·5°, $[\alpha]_D$ +84·5° (*c* 0·85, $CHCl_3$). (Found: C, 48·76; H, 3·62; N, 19·12. $C_{12}H_{11}ClN_4O_3$ requires: C, 48·89; H, 3·73; N, 19·01%).

6-*Chloro*-9-(4'-O-*acetyl*-2',3'-*dideoxy*-α-L-glycero-*pent*-2'-*enosyl*) *purine* (IV'). The next band gave 0·27 g of a syrup which could not be crystallized, $[\alpha]_D$ −72·4° (*c* ~1·0, $CHCl_3$). (Found: M^+ 294; 296. $C_{12}H_{11}ClN_4O_3$ requires: M.W. 294; 296).

6-*Chloro*-9-(3',4'-*di*-O-*acetyl*-2'-*deoxy*-β-L-erythro-*pentopyranosyl*)*purine* (IX) *and* 6-*chloro*-9-(4'-O-*acetyl*-2',3'-*dideoxy*-β-L-glycero-*pent*-2'-*enosyl*) *purine* (V'). The product obtained from the other band 0·91 g, was dissolved in boiling MeOH. The soln was kept overnight at room temp and the crystalline ppt obtained (0·5 g) was collected and recrystallized from the same solvent to give a solid, IX, m.p. 203–205°; $[\alpha]_D$ −21·3° (*c* 0·8, acetone); λ_{max}^{EtOH}, 263 mμ (ε 9330); λ_{max}^{EtOH}, pH 1; 263 mμ (ε 9330); λ_{max}^{EtOH}, pH 11; 264 (ε 9330). (Found: C, 47·32; H, 4·20; N, 15·78. $C_{14}H_{15}ClN_4O_5$ requires: C, 47·40; H, 4·23; N, 15·80%). Compare with compound described[3] as 6-chloro-9-(3',4'-di-O-acetyl-2'-deoxy-α-D-ribopyranosyl) purine, m.p. 205–207°, $[\alpha]_D$ +21·8° (*c* 0·75, acetone).

The solid obtained by evaporation of the combined filtrates was recrystallized two times from MeOH to give V' as a crystalline solid, m.p. 101–102°; $[\alpha]_D$ −148·2° (*c* 1, $CHCl_3$). (Found: C, 47·41; H, 3·85; N, 18·47. $C_{12}H_{11}ClN_4O_3 \cdot \frac{1}{2}H_2O$ requires: C, 47·47; H, 3·95; N, 18·45%).

6-*Chloro*-9-(3',4'-*di*-O-*acetyl*-2'-*deoxy*-α-L-erythro-*pentopyranosyl*)*purine* (VIII). The slower moving band afforded 0·44 g of a mixture of two products which were separated by thick-layer chromatography (silica gel PF_{254}, Merck, AcOEt). The slower moving band gave 6-chloropurine. From the faster moving band 0·24 g of a solid were obtained. Crystallization of this material from MeOH gave VIII, m.p. 149–150°; $[\alpha]_D$ +33·5° (*c* 0·7, EtOAc); λ_{max}^{EtOH}, 263 mμ (ε 8800); λ_{max}^{EtOH}, pH 1; 263 (ε 8950); λ_{max}^{EtOH}, pH 11; 263 (ε 8650). (Found: C, 47·38; H, 4·25; N, 15·84. $C_{14}H_{15}ClN_4O_5$ requires: C, 47·40; H, 4·23; N, 15·80%). Compare with compound described[3] as 6-chloro-9-(3',4'-di-O-acetyl-2'-deoxy-β-D-ribopyranosyl) purine m.p. 149–150°, $[\alpha]_D$ −33·6° (*c* 1·0, EtOAc).

Catalytic hydrogenation of III. A soln of 0·1 g of III in 20 ml AcOH was hydrogenated at ~3 atm over PtO_2 for 3 hr. The catalyst was separated by filtration and the filtrate evaporated to yield a syrup. Pure VII could be obtained by thick-layer chromatographic purification using EtOAc–cyclohexane (1:1) for development (M^+ 296; 298. $C_{12}H_{13}ClN_4O_3$ requires: M.W. 296; 298).

Acknowledgements- We thank Professor M. Lora-Tamayo for his encouragement and assistance, and to Dr L. Castedo (University Chemical Laboratory, Cambridge) for NMR (100 MHz) and mass spectral measurement.

This work was aided by a grant from the Fondo Nacional para el Fomento de la Investigación.

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