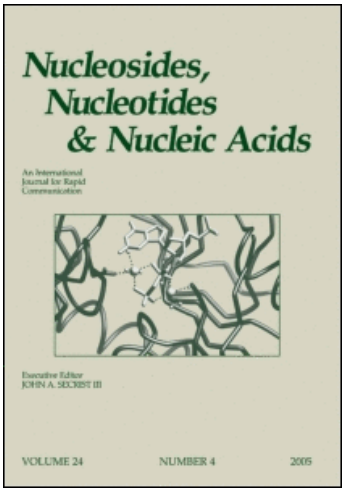

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DETERMINATION OF THE ANOMERIC CONFIGURATION OF C-NUCLEOSIDES BY ^{1}H and ^{13}C NMR SPECTROSCOPY

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CONTENTS

1. Introduction

Since the discovery by Cohn[1] in 1959 of the first C-nucleoside pseudouridine, an isolate from t-RNA hydrolysates, a number of biologically interesting C-nucleosides [formycin, formycin B, oxoformycin, oxazinomycin (minimycin), showdomycin, pyrazofurin, and several derivatives of pseudouridine] have been isolated from the culture filtrates of various micro-organisms, and their structures have been elucidated. Several review articles dealing with the chemistry and/or biology of C-nucleosides have appeared.[2-5]

Due to significant antitumor and antiviral activities[5] exhibited by these C-nucleosides, a great deal of synthetic effort has been devoted

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to the synthesis of naturally occurring C-nucleosides.[2-4] Various analogs have also been synthesized in efforts to find new and more potent chemotherapeutic agents.

The unique structural feature that distinguishes the C-nucleosides from the N-nucleosides is the presence of a carbon-carbon linkage in place of the usual carbon-nitrogen linkage between the aglycon and sugar moieties. Synthesis of C-nucleosides is deceptively difficult because of this feature, and in part, because of their facile anomerization during the synthesis as well as the absence of a good general synthetic route. Nevertheless, a number of useful intermediates have been developed for the synthesis of various types of C-nucleosides.[6-13,81-84]

A number of synthetic C-nucleosides have been prepared during the past ten years. Despite the fact that their NMR characteristics are somewhat different from those of N-nucleosides, review articles dealing with the assignment of anomeric configuration have not appeared in the literature. This report summarizes the various methods used for the assignment of the anomeric configuration of C-nucleosides based on published data as well as on our experience in C-nucleoside chemistry.

2. 2',3'-O-Isopropylidene Group Protected D-Ribofuranosyl C-Nucleosides

For pyrimidine C-nucleosides protected with the 2',3'-O-isopropylidene group, there are two basic criteria which have been successfully utilized for assignment of anomeric configuration: chemical shift (H-1') and the Imbach rule.

The chemical shifts for the anomeric protons (H-1'), being used extensively in N-nucleoside anomeric assignments,[14] have also proven to be useful in C-nucleoside assignments. The use of chemical shift data relies upon the observation that the α-anomeric proton consistently appears at lower field (higher δ) than the corresponding β-anomeric proton. This effect can be attributed to the shielding effect of a cis-hydroxy group as observed for N-nucleosides.[14] Examples of assignments made for anomeric pairs using this method include compounds 1, 2, 3, 10, 11, and 12 in which the α-anomers consistently resonated at lower field than the β-anomers. This method also applies to the five-membered ring C-nucleosides (15-36) and to "purine-like" C-nucleosides (37-49) which contain the 2',3'-O-isopropylidene group.

No exceptions to this rule have been found among the known C-nucleosides protected with a 2',3'-O-isopropylidene group.

In N-nucleosides, the coupling constant for the H-1' and H-2' protons ($J_{1',2'}$) has been used along with the chemical shift data for assignment of anomeric configuration when the J value is small enough (1.0-3.5 Hz) for the β-anomer.[14] Karplus' equation or its modification predicts that the observed coupling constant will have a value of about 3.5-8.0 and 0.0-8.0 Hz for the α- and β-anomer, respectively. The $J_{1',2'}$ values have been shown to be solvent dependent.[14]

H-1', H-2' coupling constants ($J_{1',2'}$) for protected C-nucleosides have not been found useful for anomeric configurational assignments because in some cases the anomeric proton peaks tend to overlap with those H-2' and H-3' protons and because $J_{1',2'}$ values of the β-D configuration are not consistently smaller than those of the α-D configuration. As an example, compound 12 shows a $J_{1',2'}$ = 4.6 Hz and 3.6 Hz for the α- and β-anomers, respectively, whereas compound 16 shows a value of 3.1 and 4.6 Hz for the anomers. In free C-nucleosides, however, $J_{1',2'}$ coupling constants provide valuable information for assignment of configuration (Table 3).

Another convenient method for assigning anomeric configuration involves use of the Imbach rule. This method has been successfully applied to N-nucleosides[15-17] although exceptions to this rule have recently been reported.[80] The Imbach rule is based on the difference in chemical shift values ($\Delta\delta$) between the endo- and exo-methyl group of the isopropylidene moiety as a 2',3'-hydroxyl protecting group of ribose. The difference observed is usually <0.15 and >0.15 ppm for the α-D and β-D anomers, respectively. Even before the Imbach rule was formulated, this difference had been observed.[14] Imbach and co-workers suggested that this difference could be attributed to the anisotropic effect of the heterocyclic ring on endo methyl groups in an α-anomer. This argument has been substantiated by data on those 2',3'-O-isopropylidene-D-ribofuranosyl derivatives which do not have heterocyclic aglycons and thus do not comply with these criteria.[34]

The Imbach rule appears to be a reliable method for determining the anomeric configuration of 2',3'-O-isopropylidene group protected pyrimidine-C-nucleosides despite the trityl group substitution at the 5'-position of the ribose. According to Imbach,[34] 5'-position substitution causes ring deformation and he recommended that the rule

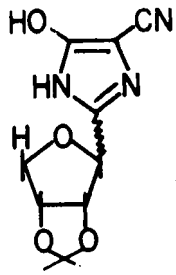
not be applied under those circumstances. Compound 1, 2, 10, 11, and 12 consistently follow the rule that α- and β-anomers exhibit Δδ 0.02-0.14 and 0.16-0.23 ppm, respectively. The rule is even useful when only one anomer is available during a synthesis. For example, 5-(2 ,3 -O-isopropylidene-5 -O-trityl-α-D-ribofuranosyl)isocytidine (7), which was obtained as the only C-nucleoside product from the condensation of ethyl 3-methoxy-2-(2,3-O-isopropylidene-5-O-trityl-D-ribofuranosyl)-acrylate and guanidine, gave a Δδ value of 0.11 ppm. According to Imbach's rule, this compound falls into the range assigned for α-anomer. This assignment proved to be accurate.[8] Compound 9, also obtained as an only product, gave a Δδ value of 0.23 ppm. The assignment of a configuration based on the Imbach rule was later shown to be accurate on the basis of $J_{3',4'}$ = 3 Hz and other features of the spectrum.[18] The Imbach rule has therefore proven to be a very useful tool for assignment of anomeric configuration of protected pyrimidine-C-nucleosides (Table 1) with one exception (see compound 3). In this case assignment of configuration relied on the chemical shift (H-1') data and on the deblocked nucleoside.

The Imbach rule has also been found convenient for anomeric assignment of five-membered ring C-nucleosides (15-36). Although the strict sense of Imbach's rule (Δδ <0.15 for α and Δδ >0.15 for β) is not applicable, the general trend of Δδ values between α- and β-anomers still held. For example, 3-aminopyrazole-C-nucleoside 15 gave Δδ 0.19 and 0.22 for the α- and β-anomers, respectively. The Δδ 0.19 is considerably higher than that of Imbach's rule but is, nevertheless smaller than that for the β-anomer. It is to be emphasized, however, that caution should be exercised whenever only a single anomer is available for analysis unless the observed value is very low for the α-anomer or very high for the β-anomer. Values for the α-(17-19) and the β-(32) isomers were observed as high as Δδ 0.21 and as low as Δδ 0.19, respectively. Nevertheless, for compounds 26-29, the values were high enough to permit assignment as the β-anomers and were thus consistent with concept of Imbach. The original assignments of these compounds, however, were based on the known anomeric configuration of the starting material.[35] It is interesting to note that the nucleosides 26-29 display extremely high δ values (5.43-5.84 ppm) for H-1' when compared to other β-anomers (4.5-5.0 ppm). This may be attributed to the deshielding effect of the carbonyl group adjacent to the anomeric

proton. In the case of compound 35, the Imbach rule or a modification thereof alone will not permit an unambigous assignment of the configuration because the same $\Delta\delta$ value (0.24 ppm) is exhibited by both α- and β-anomers. Thus, Cousineau and Secrist[27] assigned the anomeric configuration of 35 on the basis of ^{13}C NMR shift data, comparison of H-1' chemical shift, and shape of the H-4' signal.

It has been observed[18] that the isopropylidene methyl group signals occur at 25.5 ± 0.2 and 27.5 ± 0.2 ppm for the β-anomer and at 24.9 ± 0.3 and 26.3 ± 0.2 for the α-anomer. Compound 35 thus was found to resonate at 25.68 and 27.62 ppm for the β-anomer and 25.10 and 26.41 ppm for the α-anomer. These data are consistant with the above observation.[18] In addition, it was observed that for similar compounds in the study, ^{13}C $\Delta\delta$ for these two methyl groups was 1.90 ± 0.2 and 1.25 ± 0.2 ppm for the α- and β-anomers, respectively. This is consistent with 35 ($\Delta\delta$ 1.94 ppm for the β- and 1.31 ppm for the α-anomer). Further support for the configurational assignment came from an examination of the chemical shift of the central (or quaternary) isopropylidene carbon. From the study of over 60 examples, they[27] were able to ascertain that these resonances usually appear at 114.5 ± 0.6 ppm for the β-anomer and at 112.7 ± 0.6 ppm for the α-anomer. The values obtained for 35 (114.77 and 112.97 ppm) were, therefore, consistent with the (δ5.56). Additionally, the above mentioned effect (values) may also be attributed to the electron withdrawing effect of acyl groups at H-2'.

The preceding discussion has focused on the utility of ^{1}H NMR spectroscopy in determining the anomeric configuration of C-nucleosides. ^{13}C NMR spectroscopy has also been applied, as briefly mentioned (page 5),to the problem of establishing the configurations of the sugar intermediates,[18] pyrazole C-nucleosides,[21] thiazole-C-nucleosides,[27] showdomycin analogs,[22] and imidazole-C-nucleosides.[23] It has been established[18] that the chemical shifts of carbon atoms are extremely sensitive to steric crowding, especially by vicinal oxygen substituents. Thus, sterically crowded carbons resonate at higher field (lower ppm) than in the absence of steric crowding. This shielding effect has been observed in furanose sugars[24] and the chemical shift of the anomeric carbon atoms has also been used to distinguish between α- and β-furanosides in both O-glycosides[25] and nucleosides.[26] The signal of that isomer having a cis relationship between the aglycon and its C-2 hydroxyl group will appear at higher field.

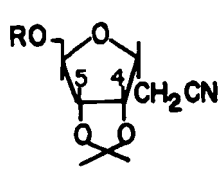


C-α
D-β

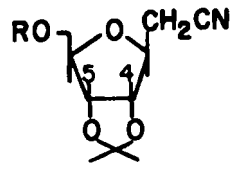
For example, the signal due to C-1' in the ^{13}C NMR spectrum of the α-anomer of compound C appeared at lower field (83.91 ppm) than did the β-anomer D (81.24)[23]. The anomeric configurational assignment was confirmed using the Imbach rule. Moffatt and co-workers[22] also assigned the configuration of compound 33 on the basis of ^{13}C chemical shifts for the isopropylidene methyl groups. They observed that the ^{13}C chemical shifts for the methyl groups in the 2',3'-O-isopropylidene derivatives above data for β- and α-anomers, respectively. Furthermore, the chemical shifts of anomeric protons (δ4.94 for a β-anomer and 5.30 for an α-anomer) assured an unambiguous assignment for the anomeric configuration of compound 35.

It has been observed that for "purine-like" C-nucleosides with 2',3'-O-isopropylidene as well as 5'-O-trityl groups substituted D-ribose, the difference in chemical shift values (Δδ) between the endo- and exo-methyl groups of the isopropylidene moiety do not provide any helpful information for assignment of the anomeric configuration despite the usefulness of the rule in pyrimidine C-nucleosides with the same protecting groups of the ribose moiety. This may be attributed to anisotropic effects of the trityl group as originally indicated by Imbach.[34] For example, compound 38 (Δδ 0.23 ppm for both anomers) and 39 (Δδ 0.24 ppm for both anomers) exhibit no difference. Chemical shift data for the H-1' proton in these nucleosides do, however, provide a reliable tool for determining the configurational assignments.

In addition to the chemical shift method, the $J_{3',4'}$ coupling constants (or $J_{5,6}$ for the structures shown in A and B, below) have been used for the assignment of anomeric configurations of pyrimidines,[19] "purine-like"[20] C-nucleosides, and sugar intermediates.[18]



A



B

From their study of furanosyl C-glycosides, Moffatt and co-workers[18] observed that the β-anomer B gave a value of $J_{5,6}$ = 4-5 Hz while the α-anomer A exhibited a $J_{5,6}$ = 0-1 Hz. X-Ray crystal studies of an α-anomer revealed that the furanose ring adopts a configuration in which C_3, C_4, C_5 and C_6 are essentially planar and the ring oxygen is puckered, projecting into an endo oriented envelope. Examination of Dreiding models showed that such a conformation results in a dihedral angle between H-5 and H-6 of about 90°, which is consistent with the very small observed coupling constant. Therefore, Moffatt and co-workers suggested that the β-C-glycosides adopt an alternate O-exo envelope conformation in which the steric interaction between these substituent groups is relieved and the dihedral angle is about 160°. This value is compatible with the observed value of $J_{5,6}$ of 4-5 Hz. This criterion, along with the chemical shifts of H-1', were utilized for the assignment of pyrimidine 12 and purine nucleosides 111 and 112, in which β-anomer showed well-resolved sugar proton spectra while the spectral peaks for H-3' and H-4' protons are collapsed for the α-anomer (i.e., $J_{3',4'}$ = about 0 Hz). The same phenomena have been observed in N-nucleosides resulting in an "apparent triplet" resonance peak for H-4'.[85]

3. Acyl or Benzyl Group Protected C-Nucleosides

Although it is quite convenient to start from 2,3-O-isopropylidene-5-O-tritylribofuranose, acetyl, benzoyl or benzyl protected D-ribose have also been used for C-nucleoside syntheses. For these compounds (50-63), most of the assignments of anomeric configuration at the protected stage were made on the basis of the starting materials for which the anomeric configuration had previously been established. No general criteria have been established for the direct assignment of

these nucleosides. Furthermore, the assignment based on the chemical shifts of H-1' do not seem plausible for these compounds. For example, anomeric pair 52 behaves differently from other pairs of protected C-nucleosides. This may be rationalized on the basis of the deshielding effect of the carbonyl group by which the H-1' proton in the β-anomer is influenced more than that of the α-anomer. The Dreiding models reveal the the H-1' proton of the β-anomer lies near the carbonyl group while the same proton in the α-anomer does not. Consequently, H-1' of the β-anomer resonates at lower field (δ5.62) than the corresponding α-anomer of a variety of C-glycosides appear at 25.5 ± 0.2 and 27.5 ± 0.2 for the β-anomers and at 24.9 ± 0.2 and 26.3 ± 0.2 for the α-anomers. For compound 33, the observed values were 25.49 and 27.83 ppm while those for 2,3'-O-isopropylideneshowdomycin were 25.43 and 27.60 ppm. Both sets of data were in good agreement with the β-configuration. As previously discussed, for compound 35, Moffatt and co-workers[22] used the ^{13}C chemical shifts of the central isopropylidene carbon which appears at 114.53 ppm as a critical piece of evidence in their studies. This chemical shift was consistent with other data. Although only one anomer was available for assignment, ^{13}C NMR spectroscopic data, the Imbach rule, and the chemical shift data for the H-1' proton combined to allow assignment of the anomeric configuration of 33 with a reasonable degree of confidence. The use of ^{13}C NMR data failed to make an assignment in some cases involving carbohydrate intermediates.[21]

4. Free D-Ribofuranosyl-C-Nucleosides

The most reliable and convenient method for assignment of anomeric configurations for free C-nucleosides is the use of differences in H-1' chemical shifts. As previously discussed, the H-1' proton of β-anomers appear at higher field than those of α-anomers due to the shielding effects of a cis 2'-hydroxy group. This method has been extensively applied to N-nucleosides.[14] To date we have not uncovered any exceptions to this rule in the published literature. Even when only one isomer is available from the synthetic procedure, the anomeric configuration can be assigned on the basis of the chemical shift for the anomeric proton with a reasonable degree of confidence provided that similar compounds are available for comparison. Moffatt and co-workers[22] assigned the β-configuration for compound 80, for which the H-1' proton signal appeared at δ4.60. This is close to that of

showdomycin (4.53). Pyrimidine C-nucleosides have H-1' chemical shifts of δ 4.68-5.12 and 4.15-4.72 for the α- and β-anomers, respectively. These values might allow us to determine the anomeric configuration even if a single anomer should become available through synthesis provided that the chemical shift of H-1' is sufficiently low for the β and sufficiently high for the α isomer.

^{13}C NMR chemical shifts have been applied also for assignment of anomeric configuration of free nucleosides. Cousineau and Secrist[27] assigned the anomeric configuration for compound 95 on the basis of both ^{13}C and ^{1}H chemical shifts. They observed that C-1' of the α-anomer appeared at higher field (76.80 ppm) than the corresponding β-anomer (78.02 ppm). This is consistent with previous findings.[18,21]

Coupling constants of free C-nucleosides can also be useful in the assignment of anomeric configuration (64-118). It has been consistently observed that in D-ribofuranosyl-C-nucleosides, contrary to the N-nucleosides, β-anomers display, in general, larger coupling constants (3.0-7.3 Hz) than do the corresponding α-anomers (1.8-4.0 Hz), except for those C-nucleosides which do not share close structural features in common with the natural nucleosides (compounds 70, 111-113). Thus it is possible to speculate from this data that the ribose conformation of C-nucleosides is somewhat different from that of N-nucleosides although Smith and co-workers[36] suggested, based on their ^{1}H NMR study of pseudouridine, that the C-nucleoside assumes a ribose conformation almost identical to that of uridine. The above method, based on the coupling constant values together with the chemical shift data can ensure the unambiguous assignment of anomeric configuration of C-nucleosides.

As previously discussed for protected C-nucleosides, the coupling constants for H-3' and H-4' have also been utilized for assignment of anomeric configuration for compounds 112 and 113 as a complementary method. Igolen and co-workers observed [20] that the β-anomers of 112 and 113 showed well-resolved sugar protons whereas in the α-anomers H-3' and H-4' exhibit collapsed peaks.

Another technique utilized for assignment of anomeric configuration is an application of spin-lattice relaxation time (T_1) for the anomeric proton. The T_1 for β-anomers was found to be about 2.5 times longer (3.24-4.18 sec.) than for the α-anomers (1.35-1.60 sec.). From these observations, Tran-Dinh and co-workers[28] suggested that this criterion

alone may permit the unambiguous determination of anomeric configuration even if only one anomer is available.

Legraverend and co-workers[29] also used this method for assigning anomeric configuration for compound 115. Relaxation times for the α- and β-anomers were 0.85 and 2.30 seconds, respectively. However, because of the limited examples in the literature as well as the limited measurement of the relaxation time in most routine NMR studies, the validity of the method must await further tests.

5. Free 2'-Deoxy-D-ribofuranosyl-C-Nucleosides

^{1}H NMR spectroscopy has been extensively applied for the assignment of anomeric configuration of 2'-deoxy-N-nucleosides.[14] The method not only depends on the difference in peak patterns observed for the anomeric protons, but also on peak-widths observed. It has been observed that an α-D anomer displays quartet having a peak-width of 10.4 ± 0.4 Hz for H-1' whereas a β-D anomer displays a pseudotriplet having a peak width of 13.7 ± 0.5 Hz. The occurrence of a quartet rather than a pseudotriplet for the anomeric proton of certain β-anomers has been reported while peak widths have been found to be invalid for 8-substituted purine derivatives in which the free rotation is restricted because of substitution at C-8. Despite these exceptions, the empirical method may be applicable if both anomers are available for comparison in the N-nucleoside series.[14]

In C-nucleosides, a quartet for the α-anomer and a pseudotriplet for the β-anomer are not routinely found. This is probably due to the conformational change of the sugar moiety in C-nucleosides as contrasted to the N-nucleosides. It is well recognized that the bond distances between the aglycon and carbohydrate moieties in C-nucleosides are longer than those of N-nucleosides. Consequently, free rotation along the C-C axis is accelerated, relative to N-C rotation in the N-nucleosides, and may account for the conformational changes of the carbohydrate moiety in the C-nucleosides.

The ^{1}H NMR spectral patterns exhibited by anomeric protons of 2'-deoxy-D-ribofuranosyl-C-nucleosides 120, 122, 128 and 129 are all quartets whereas compounds 119, 121, and 127 (all β-anomers) exhibit pseudotriplets. The triplet pattern is consistent with 2'-deoxy-β-D-ribofuranosyl-N-nucleosides. For compounds 123, 130, 131, and 132, however, both α- and β-anomers exhibit quartets (double doublets). It

is consequently difficult to assign the anomeric configuration of 2'-deoxy-D-ribofuranosyl-C-nucleosides on the basis of splitting patterns (the quartet-triplet principle[63]). In an effort to devise a reliable method, Igolen and co-workers[31] found that the sum, $J_{1',2'} + J_{1',2''}$, was useful. They observed that for compound 124, the H-1' signal was broader for the β-anomer (summed J values = 15.3 Hz) than for the corresponding α-anomer (summed J values = 14.0 Hz). The same trend was also noted for compounds 130, 131, and 132.[32]

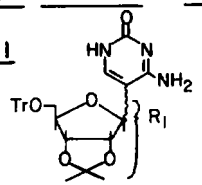
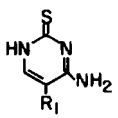
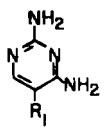
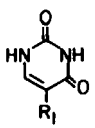
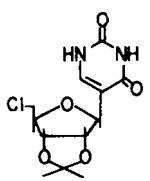
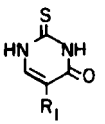
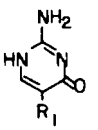
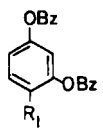
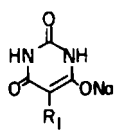
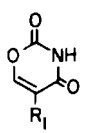
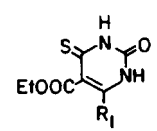
Another method of assignment of anomeric configuration was proposed by Srivastava and Robins.[13] They observed that the absorption of H-2', H-2" for α-anomers extends to both higher and lower fields, providing a large absorption band width (1.12-1.00 ppm) as compared to the corresponding β-anomer (0.02-0.63 ppm). They suggested that a relatively large band width of Δδ 2', 2", observed for the α-anomer as compared to that of the β-anomer, is due to the spacing of H-2' (trans to the thiazole ring) in an equatorial orientation of the puckered furanose ring and in the deshielding region of the thiazole ring. Consequently, H-2' appears at lower field compared to that of H-2" (trans to H-1'), which is shielded by the cis 3'-hydroxy group and the cis-thiazole ring.

6. Free D-Arabinofuranosyl-C-Nucleosides

For D-arabinofuranosyl-C-nucleosides, as for pentofuranose derivatives,[78] the order of H-1' chemical shifts is reversed to that of D-ribofuranosyl nucleosides in which the α-anomer appears at higher field than the corresponding β-anomer.[74] The explanation for this is that the hydroxyl configuration in D-arabinofuranose, which exerts a shielding effect on the cis-hydrogen of the α-anomer, is reversed. Thus, 5-(β-D-arabinofuranosyl)isocytidine[74] (133) exhibits an anomeric chemical shift value of 4.67 and 5.02 ppm for α and β, respectively. These data are also consistent with the data for ara-oxoformycin (140) for which α and β signals appear at δ 5.02 and 5.28, respectively. The same trend can be seen for other pairs of arabinofuranosyl-C-nucleosides (see compounds 138-139). Although these examples are the only ones for which ^{1}H NMR data have been reported, the validity of this method for assigning anomeric configuration seems assured based on experience in the N-nucleoside field. Ferris and co-workers[23] also studied the ^{13}C chemical shifts for free arabinofuranosyl-C-nucleosides 137 and 138.

TABLE I

2',3'-O-ISOPROPYLIDENE GROUP PROTECTED C-NUCLEOSIDES

Cpd.	Structure	Anomer	Δδ	$J_{1',2'}$(Hz)	$H_{1'}$(δ)	Sol.	Ref.
1		α	0.04	—	5.44	B	9
		β	0.16	—	5.34	B	9
2		α	0.11	—	4.79	B	9
		β	0.23	—	4.67	B	9
3		α	0.21	3.4	5.19	A	9
		β	0.21	—	4.56	A	9
4		β	0.24	—	4.99	A	8
5		β	0.21	—	≤ 4.75	B	38
6		β	0.23	2.8	4.89	A[a]	8
7		α	0.11	3.5	4.96	B	8,37
8		β	0.23	—	5.10(s)[b]	B	39
9		β	0.23	—	5.05(s)	B	40
10		α	0.10	—	4.93(d)	B	51
		β	0.22	—	≤ 4.83	B	51
11		α	0.14	4.6	5.40(d)	A	19
		β	0.20	—	4.90(m)	A	19

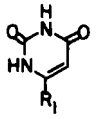
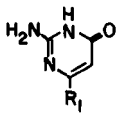
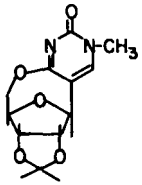
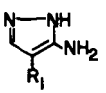
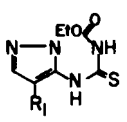
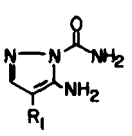
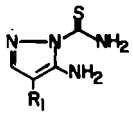
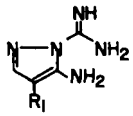
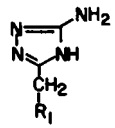
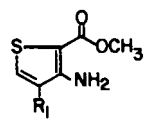
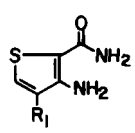
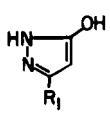
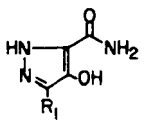
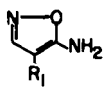
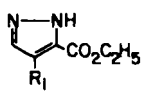
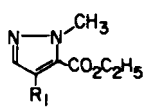
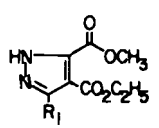
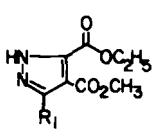
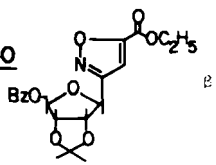
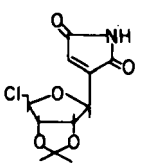
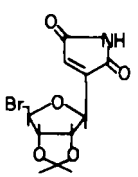
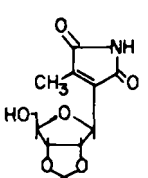
12		α	0.02	4.6	4.92(d)	B	19
		β	0.22	3.6	4.69(d)	B	19
13		β	0.22	3.0	4.52(d)	B	19
14		β	0.15	—	4.76(s)	B	41
15		α	0.19	2.2	5.15	A	42
		β	0.22	—	4.76	A	42
16		α	0.09	3.1	5.43	A	42
		β	0.23	4.6	5.00	A	42
17		α	0.21	2.4	5.07(d)	A	43
		β	0.22	—	≤ 4.80	A	43
18		α	0.21	2.7	5.09(d)	A	44
		β	0.22	2.7	4.76(m)	A	44
19		α	0.21	—	5.08(d)	A	45
		β	0.22	—	≤ 4.76(m)	A	45
20		β	0.28	—	—	D	48
21		α	0.13	3.7	5.18(d)	A	47
		β	0.24	—	≤ 4.76	A	47
22		α	0.13	4.0	5.19(d)	A	47
		β	0.25	—	≤ 4.75	A	47
23		β	0.22	—	—	A	49

Table 1 continued

Table 1 continued

Cpd.	Structure	Anomer	Δδ	$J_{1',2'}$ (Hz)	$H_{1'}$ (δ)	Sol.	Ref.
24		α	0.17	3.0	5.26(d)	D	50
		β	0.21	—	4.99(s)	D	50
25		α	0.20	—	4.72(d)	B	51
		β	0.22	—	—	B	51
26		β	0.27	2.4	5.84(d)	A	36
27		β	0.27	2.8	5.43(d)	A	36
28		β	0.26	2.4	5.55(d)	A	36
29		β	0.26	2.8	5.52(d)	A	36
30		β	0.21	—	4.83(m)	A	52
31		β	0.21	—	4.93(d)	B	53
32		β	0.19	—	4.92(d)	B	53
33		β	0.24	—	≤ 4.47	A	22

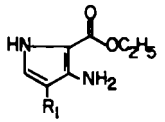
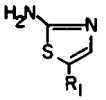
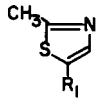
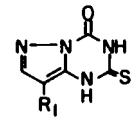
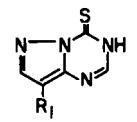
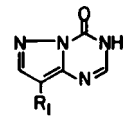
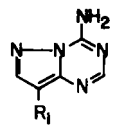
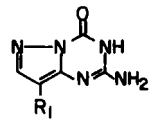
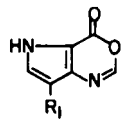
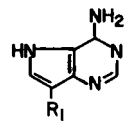
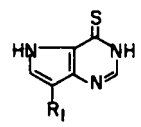
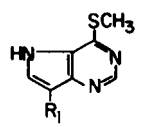
34		α	0.20	—	5.14(d)	A	57
		β	0.23	—	≤ 4.80	A	57
35		α	0.24	2.0	5.30(d)	A	27
		β	0.24	5.0	4.94(d)	A	27
36		β	0.25	4.0	5.00(d)	A	27
37		α	0.24	2.7	5.23	A	42
		β	0.25	5.0	4.92	A	42
38		α	0.23	—	5.41(d)	B	54
		β	0.23	—	5.05(s)	B	54
39		α	0.24	2.7	5.50(d)	A	55
		β	0.24	—	≤ 5.21	A	55
40		α	0.26	—	5.55(s)	A	55
		β	0.24	—	≤ 5.26	A	55
41		β	0.24	—	≤ 5.26	B	56
42		α	0.22	3.1	5.57(d)	A	57
		β	0.23	4.0	5.32(d)	A	57
43		α	0.19	3.1	5.49(d)	A	58
		β	0.20	4.3	5.22(d)	A	58
44		β	0.24	4.3	5.27(d)	A	57
45		β	0.24	4.3	5.33(d)	A	57

Table 1 continued

Table 1 continued

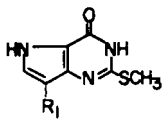
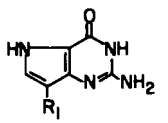
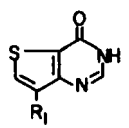
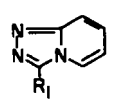
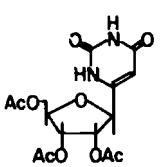
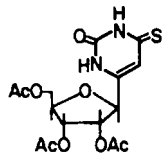
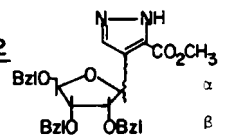
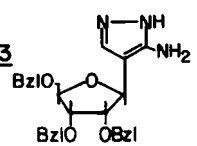
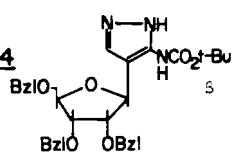
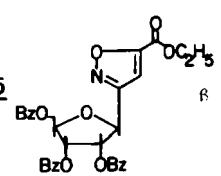
Cpd.	Structure	Anomer	Δδ	$J_{1',2'}$ (Hz)	$H_{1'}$ (δ)	Sol.	Ref.
46		β	0.26	—	≤ 5.26	A	57
47		β	0.20	—	≤ 4.99	A	57
48		α	0.12	4.3	5.70(d)	A	47
		β	0.24	2.8	5.49	A	47
49		α	0.12	4.2	5.81	—	46
		β	0.17	3.8	5.53	—	46

TABLE 2
ACYL or BENZYL PROTECTED C-NUCLEOSIDES

Cpd.	Structure	Anomer	Δδ	$J_{1',2'}$ (Hz)	$H_{1'}$ (δ)	Sol.	Ref.
50		β	—	4.7	4.72(d)	A	19
51		β	—	4.8	4.72(d)	A	19
52		α	—	2.5	5.56(d)	A	21
		β	—	2.0	5.62(d)	A	21
53		β	—	—	4.94(d)	A	21
54		β	—	6.5	5.04(d)	A	21
55		β	—	—	5.47(m)	A	52

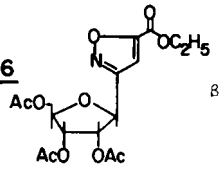
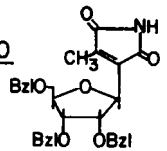
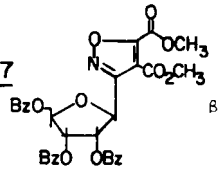
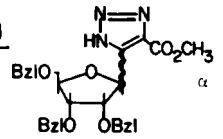
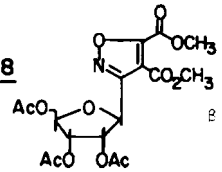
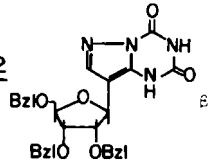
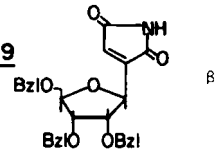
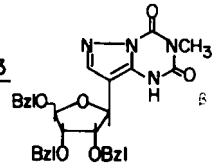
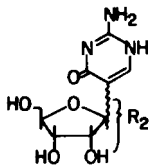
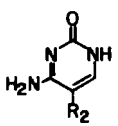
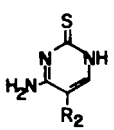
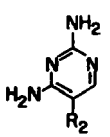
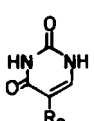
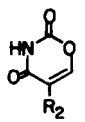
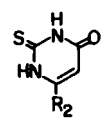
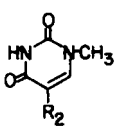
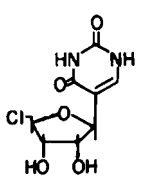
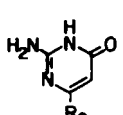
56 	β	—	—	5.34(s)	A	52	**60** 	β	—	6.0	4.91(d)	A	22
57 	β	—	4.5	5.65(d)	A	52	**61** 	α	—	5.0	5.68(d)	A	59
58 	β	—	5.5	5.36(d)	A	52	**62** 	β	—	4.0	5.00(d)	A	21
59 	β	—	2.0	4.96(dd)	A	6	**63** 	β	—	7.5	5.09(d)	A	21

TABLE 3
FREE D-RIBOFURANOSYL-C-NUCLEOSIDES

Cpd	Structure	Anomer	$J_{1',2'}$(Hz)	$H_{1'}$(δ)	Sol.	Ref.
64		α	—	5.04(d)	C	8.37
		β	—	4.72(d)	C	8.37
65		α	2.5	4.92(d)	C	60
		β	—	4.55(m)	C	60
66		α	—	5.10	C	9
		β	—	4.15	C	9
67		α	3.3	5.05	C	9
		β	—	4.63	B	9
68		α	3.3 (3.0)	5.00 (5.62)	C (E)	36 (61)
		β	5.0 (4.5)	4.67 (5.43)	C (E)	36 (61)
69		α	3.0	5.12(dd)	C	51
		β	5.0	4.72(d)	C	51
70		α	4.0	4.68(dd)	B	19
		β	4.0	4.46	B	19
71		β	4.0	4.50(d)	B	62, 64
72		β	3.9	≤ 4.59	B	38
73		β	3.0	4.25(d)	B	19

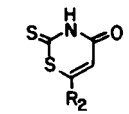
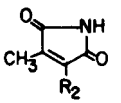
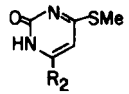
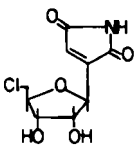
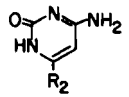
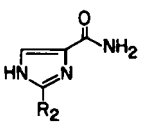
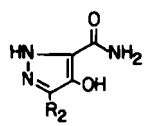
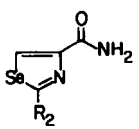
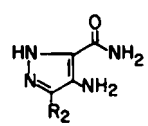
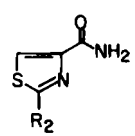
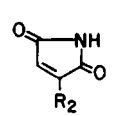
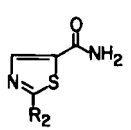
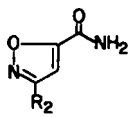
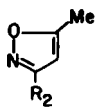
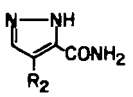
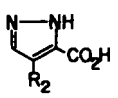
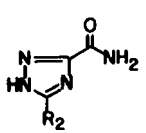
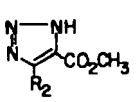
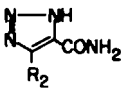
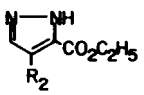
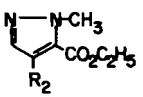
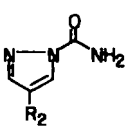
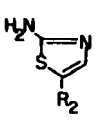
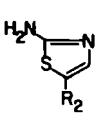
74		β	6.4	4.45(d)	B	19	**80**		β	6.8	4.60(d)	B	22
75		β	5.5	4.42(d)	B	19	**81**		β	—	4.78(d)	B	53
76		β	5.5	4.29(d)	B	19	**82**		β	6.1	5.03(d)	C	31
77		α β	3.0(3.0) 7.0(6.5)	5.83(5.68) 5.54(5.42)	$D_2O(D_2O)$ $D_2O(D_2O)$	50(65) 50(65)	**83**		α β	2.7 4.7	5.12(s) 4.88(d)	B B	33 33
78		β	6.5	4.71(d)	B	66.67	**84**		α β	3.5 5.0	5.30(d) 4.99(d)	B B	69 69
79		β	3.0	4.63(dd)	B	68	**84a**		β	5.0	4.97(d)	B	69

Table 3 continued

Table 3 continued

Cpd.	Structure	Anomer	$J_{1',2'}$(Hz)	$H_{1'}$ (δ)	Sol.	Ref.
85		β	5.5	4.71(d)	B	52
86		β	6.0	4.70(d)	B	52
87		β	—	5.95(d)	E	7
88		β	7.5	5.00(d)	B	7
89		β	6.1	5.03(d)	C	31
90		β	5.2	5.23(d)	B	35
91		β	4.6	5.27(d)	B	35
92		β	3.7	5.09(d)	B	35
93		β	4.6	5.06(d)	B	35
94		α	—	4.24(s)	B	43
		β	—	4.20(d)	B	43
95		α	3.0	5.05(d)	B	27
		β	6.0	4.70(d)	B	27
96		β	6.0	4.81(d)	B	27

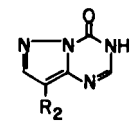
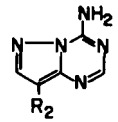
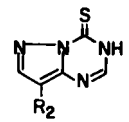
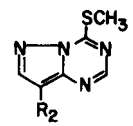
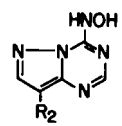
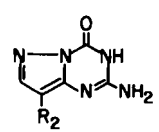
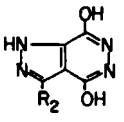
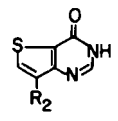
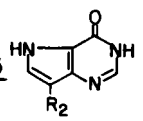
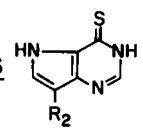
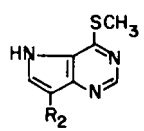
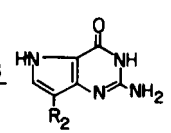
97		α	3.4	5.13(d)	B	55
		β	—	4.79(d)	B	55
98		α	3.1	5.21(d)	B	55
		β	7.0	4.83(d)	B	55
99		α	3.3	5.17(d)	B	54
		β	6.7	4.82(d)	B	56
100		β	6.4	4.92(d)	B	56
101		β	7.0	4.74(d)	B	56
102		β	6.4	4.63	B	56
103		β	7.0	5.02	B	70
104		α	1.8	5.24(d)	B	47
		β	5.8	4.97(d)	B	47
105		β	—	5.02(m)	C	57
106		β	7.0	5.06	C	57
107		β	—	5.12(m)	C	57
108		β	7.3	4.90(d)	C	57

Table 3 continued

Table 3 continued

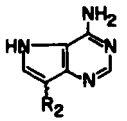
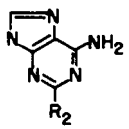
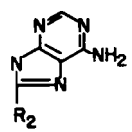
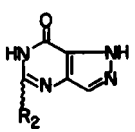
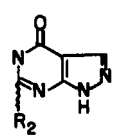
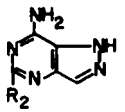
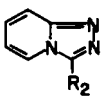
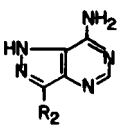
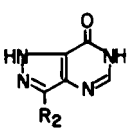
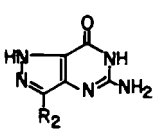
Cpd.	Structure	Anomer	$J_{1',2'}$(Hz)	$H_{1'}$(δ)	Sol.	Ref.
109		α	3.1	5.15(d)	B	58
		β	6.4	4.88(d)	B	58
110		β	4.3	4.74(d)	B/C	11
111		β	5.8	4.91(d)	B/C	11
112		α	4.9	4.87	B	20
		β	4.0	4.65	B	20
113		α	4.5	4.90	B	20
		β	4.2	4.65	B	20
114		α	5.3	4.90	B	28
		β	3.4	4.67	B	28
115		α	3.5	5.58	B	46
		β	6.9	5.21	B	46
116		β	7.2(7.6)	4.95(5.22)	B(C)	28
117		β	—	5.06(d)	B/F	79
118		β	6.0	4.80(d)	B	67

TABLE 4
FREE 2'-DEOXY-D-RIBOFURANOSYL-C-NUCLEOSIDES

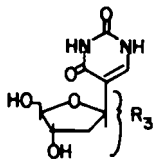
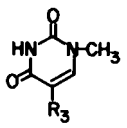
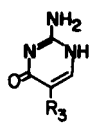
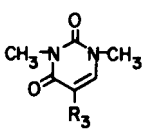
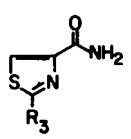
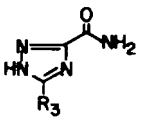
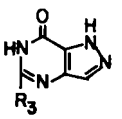
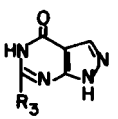
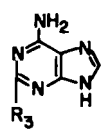
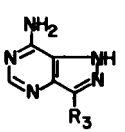
Cpd.	Structure	Anomer	$H_{1'}(\delta)$	$J_{1'2'}$(Hz)	$J_{1'2''}$(Hz)	Sol.	Ref.
119		β	4.97(t)	8.5	7.2	C	30,31
120		β	4.81(dd)	6.1	4.1	C	30,71
121		β	4.83(t)	8.2	7.2	B	30,71
122		β	5.04(dd)	6.4	6.0	C	30,71
123		α	5.30(dd)	8.0	5.2	C	13
		β	5.30(dd)	9.0	6.2	C	13
124		α	5.13	8.7	6.6	C	31
		β	5.14	7.0	7.0	C	31
125		α	4.90	8.6	4.7	B	20
		β	4.94	8.4	7.3	B	20
126		α	4.93	8.7	4.5	B	20
		β	4.96	7.5	7.5	B	20
127		α	4.91(dd)	7.9	5.4	B	72
		β	4.99(t)	7.5	7.5	B	72
128		β	5.46(dd)	6.8	—	B	73

Table 4 continued

Table 4 continued

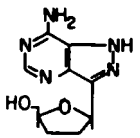
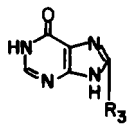
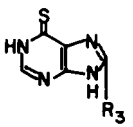
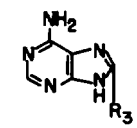
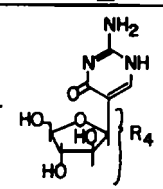
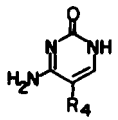
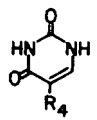
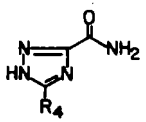
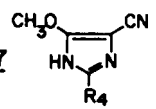
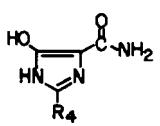
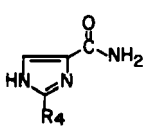
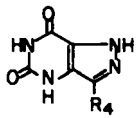
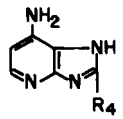
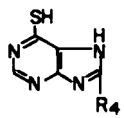
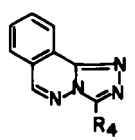
Cpd.	Structure	Anomer	$H_{1'}(\delta)$	$J_{1'2'}$(Hz)	$J_{1'2''}$(Hz)	Sol.	Ref.
129		β	5.16(dd)	6.8	—	B	73
130		α	5.13(dd)	7.5	6.0	B	32
		β	5.12(dd)	7.7	7.7	B	32
131		α	5.19(dd)	7.6	5.8	B	32
		β	5.20(dd)	8.6	6.6	B	32
132		α	5.15(dd)	7.5	6.0	B	32
		β	5.15(dd)	7.7	7.7	B	32

TABLE 5
FREE D-ARABINOFURANOSYL-C-NUCLEOSIDES

Cpd.	Structure	Anomer	$H_{1'}(\delta)$	$J_{1'2'}$(Hz)	$J_{1'2''}$(Hz)	Sol.	Ref.
133		α	4.67(q)	6.1	—	C	74
		β	5.02	3.7	—	C	74
134		β	4.97(d)	4.2	—	C	74
135		β	5.01(d)	3.6	—	C	74
136		α	4.76	6.0	—	B	31
137		α	≤4.20	—	—	—	23
		β	4.66	—	—	—	23
138		α	≤4.20	—	—	—	23
		β	4.62	—	—	—	23
139		α	≤4.10	—	—	—	23
		β	4.67	—	—	—	23

140		α	5.02(d)	6.5	—	C	75
		β	5.28(d)	6.5	—	C	75
141		α	4.88(d)	6.5	—	B	76
142		α	4.81(d)	5.5	—	B	76
143		α	5.70	5.0	—	B	77

[a] A = $CDCl_3$, B = DMSO-d_6, C = D_2O, D = CD_3OD, E = Pyridine-d_5, F = DAc

[b] s = singlet, d = doublet, t = triplet
dd = double doublet, m = multiplet
q = quartet

The results appear, however, to be inconsistent. In compound 137, 76.48 ppm (C-1') was listed for the α-anomer and 71.72 ppm (C-1') for the β-anomer. For 138, on the other hand, a value of 71.13 ppm was listed for the α-anomer and 76.48 for the β-anomer. This reversal of the chemical shifts might be attributed to some additional steric crowding between the C-2' hydroxyl and the C-1' proton of D-arabinofuranosyl C-nucleosides.

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REFERENCES

1. Cohn, W. E., Biochim. Biophys. Acta, 1959, 32, 569.
2. Hanessian, S.; Pernet, A. G., Advan. Carbohydr. Chem. Biochem., 1976, 33, 111-118.
3. Daves, Jr., G. D.; Cheng, C. C., Progress Med. Chem., 1976, 13, 303-348.
4. James, E. R., J. Carbohydr. Nucleosides Nucleotides, 1979, 6, 417-465.
5. Suhadolnik, R. J., Nucleoside Antibiotics, Wiley-Interscience, New York, 1970; Suhadolnik, R. J., Nucleosides as Biological Probes, Wiley-Interscience, New York, 1979.
6. Trummlitz, G.; Moffatt, J. G., J. Org. Chem., 1973, 38, 1841.
7. Albrecht, H.P.; Repke, D. B.; Moffatt, J. G., J. Org. Chem., 1974, 39, 2176.
8. Chu, C. K.; Wempen, I.; Watanabe, K.A.; Fox, J. J., J. Org. Chem., 1976, 41, 2793.

9. Chu, C. K.; Reichman, U.; Watanabe, K. A.; Fox J. J., J. Org. Chem., 1977, 42, 711.
10. Tam, S. Y-K.; De Las Heras, F. G.; Klein, R. S.; Fox, J. J., Tetrahedron Letters, 1975, 3271.
11. Huynh-Dinh, T.; Kolb, A.; Gouyette, C.; Igolen, J., J. Heterocycl. Chem., 1975, 12, 111.
12. Albrecht, H. P.; Repke, D. B.; Moffatt, J. G., J. Org. Chem., 1973, 38, 1836.
13. Srivastava, P. C.; Robins, R. K., J. Heterocycl. Chem., 1981, 18, 1659.
14. Townsend, L. B., Synth. Proced. Nucleic Acid Chem., 1973, 2, 267.
15. Imbach, J. L.; Kam, B. L., J. Carbohydr. Nucleosides, Nucleotides, 1974, 1, 271.
16. Imbach, J. L.; Barascut, J.-L.; Kam, B. L.; Tapiero, C., Tetrahedron Lett., 1974, 129.
17. Imbach, J. L.; Barascut, J.-L.; Kam, B.L.; Rayner, B.; Tamby, C.; Taipero, C., J. Heterocycl. Chem., 1973, 10, 1070.
18. Ohrui, H.; Jones, G. H.; Moffatt, J. G.; Maddox, M. L.; Christensen, A. T.; Byram, S. K., J. Am. Chem. Soc., 1975, 97, 4602.
19. Tam, S. Y-K.; Klein, R.S.; De Las Heras, F. G.; Fox, J. J., J. Org. Chem., 1979, 44, 4854.
20. Huynh-Dinh, T.; Kolb, A.; Gouyette, C.; Igolen, J.; Tran-Dinh, S., J. Org. Chem., 1975, 40, 2825.
21. Gupta, C. M.; Jones, G. H.; Moffatt, J. G., J. Org. Chem., 1976, 41, 3000.
22. Trummlitz, G.; Repke, D.B.; Moffatt, J.G., J. Org. Chem., 1975, 40, 3352.
23. Ferris, J. P.; Badesha, S. S.; Ren, W. Y.; Huang, H.C.; Sorcek, R. J., J. Chem. Soc., Chem. Comm., 1981, 110.
24. Perlin, A.S.; Cyr, N.; Koch, H.J.; Korsch, B., Ann. N.Y. Acad. Sci., 1973, 222, 935.
25. Usui, T.; Tsushima, S.; Yamaoka, N.; Matsuda, K.; Tuzimura, K.; Sugiyama, H.; Seto, S.; Fuzzeda, K.; Miyajima, G., Agric. Biol. Chem., 1974, 38, 1409.

26. Sugiyama, H.; Yamaoka, N.; Shimizu, B.; Ishido, Y.; Seto, S., Bull. Chem. Soc., Jpn., 1974, 47, 1815.
27. Cousineau, T.J.; Secrist III, J.A., J. Org. Chem., 1979, 44, 4351.
28. Tran-Dinh, S.; Neumann, J.-M.; Thiery, J-M.; Huynh-Dinh, T.; Igolen, J.; Guschlbauer, W., J. Am. Chem. Soc., 1977, 99, 3267.
29. Legraverend, M.; Bisagni, E.; Lhoste, J-M., J. Heterocycl. Chem., 1981, 18, 893.
30. Chu, C. K.; Reichman, U.; Watanabe, K. A.; Fox, J. J., J. Heterocyclic Chem., 1977, 14, 1119.
31. Huynh-Dinh, T.; Igolen, J.; Bisagni, E.; Marquet, J.P.; Civier, A., J. Chem. Soc., 1977, 761.
32. Kolb, A.; Gouyette, C.; Huynh Dinh, T.; Igolen, J., Tetrahedron, 1973, 31, 2971.
33. Srivastava, P.C.; Robins, R.K., J. Med. Chem., 1983, 26, 445.
34. Imbach, J.-L., Ann. N.Y. Acad. Sci., 1975, 255, 177.
35. De Las Heras, F.G.; Tam, S. Y-K.; Klein, R.S.; Fox, J. J., J. Org. Chem., 1976, 41, 84.
36. Hruska, F. E.; Grey, A. A.; Smith, I.C.P., J. Am. Chem. Soc., 1970, 92, 4088.
37. Chu, C. K.; Watanabe. K. A.; Fox, J. J.; J. Heterocycl. Chem., 1975, 12, 817.
38. Earl, R.A.; Townsend, L.B., J. Carbohydr. Nucleosides Nucleotides, 1980, 7, 35.
39. Sharma, R. A.; Bobek, M.; Bloch, A., J. Med. Chem., 1975, 18, 473.
40. Ohrui, H.; Fox, J. J., Tetrahedron Letters, 1973, 1951.
41. Reichman, U.; Hirota, K.; Chu, C. K.; Watanabe, K. A.; Fox, J. J., J. Antibiotics, 1977, 30, 129.
42. De Las Heras, F. G.; Chu, C. K.; Tam, S. Y-K.; Klein, R. S.; Watanabe, K. A.; Fox, J. J., J. Heterocycl. Chem., 1976, 13, 175.
43. Chu, C. K.; Watanabe, K. A.; Fox, J. J., J. Heterocyclic Chem., 1980, 17, 1435.
44. Chu, C.K., submitted for publication.
45. Chu, C.K., Heterocycles, in press.

46. Huynh-Dinh, T.; Igolen, J., J. Org. Chem., 1976. 41, 3124.
47. Ren, W.-Y.; Lim., M.-I.; Otter, B. A.; Klein, R. S., J. Org. Chem., 1982, 47, 4633.
48. Gensler, W. J.; Chan, S.; Ball, D. B., J. Org. Chem., 1981, 46, 3407.
49. Kozikowski, A.P.; Goldstein, S., J. Org. Chem., 1983, 48, 1139.
50. De Bernardo, S.; Weigele, M., J. Org. Chem., 1976, 41, 287.
51. De Bernardo, S.; Weigele, M., J. Org. Chem., 1977, 42, 109.
52. Albrecht, H. P.; Repke, D B.: Moffatt, J. G., J. Org. Chem., 1975, 40, 2143.
53. Earl, R. A.; Townsend, L. B., J. Carbohydr. Nucleosides Nucleotides, 1978, 5, 305.
54. Chu, C. K., submitted for publication.
55. Tam, S. Y-K.; Klein, J. S.; De Las Heras, F. G.; Klein, R. S.; Fox, J. J., J. Heterocyclic Chem., 1976, 13, 1305.
56. Tam, S. Y-K.; Klein, R.S.; Wempen, I.; Fox, J. J., J.Org. Chem., 1979, 44, 4547.
57. Lim, M-L.; Ren, W-Y.; Otter, B. A., Klein, R. S., J. Org. Chem., 1983, 48, 780.
58. Lim, M-L.; Klein, R. S., Tetrahedron Letters, 1981, 22, 25.
59. Buchanan, J. G.; Edgar, A. R.; Power, M. J.; Williams, G. C., Carbohydr. Research, 1977, 55, 225.
60. David, S.; Lubineau, A., Carbohydr. Research, 1973, 29, 15.
61. Lerch, U.; Burdon, M. G.; Moffatt, J. G., J. Org. Chem., 1971, 36, 1507.
62. Earl, R. A.; Townsend, L. B., J. Heterocycl. Chem., 1977, 14, 699.
63. Robins, M. J.; Robins, R. K., J. Am. Chem. Soc., 1965, 87, 4934.
64. Argoudelis, A. D.; Mizsak, S. A., J. Antibiotics, 1976, 29, 818.

65. Gutowski, G. E.; Chaney, M. O.; Jones, N. D.; Hamill, R. L.; Davis, F. A.; Miller, R. D., Biochem. Biophys. Res. Comm., 1973, 51, 312.
66. Lewis, A. F.; Long, R. A.; Roti Roti, L. W.; Townsend, L. B., J. Heterocycl. Chem., 1976, 13, 1359.
67. Lewis, A. F.; Townsend, L. B., J. Am. Chem. Soc., 1982, 104, 1073.
68. Nakagawa, Y.; Kano, H.; Tsukuda, Y.; Koyama, H., Tetrahedron Letters, 1967, 4105.
69. Srivastava, P. C.; Pickering, M. V.; Allen, L. B.; Streeter, D. G.; Campbell, M. T.; Witkowski, J. T.; Sidwell, R. W.; Robins, R.K., J. Med. Chem., 1977, 20, 256.
70. Farkas, J.; Sorm. F., Coll. Czech. Chem. Comm., 1972, 37, 2798.
71. Matsuda, A.; Chu, C. K.; Reichman, U.; Pankiewicz, K.; Watanabe, K. A.; Fox, J. J., J. Org. Chem., 1981, 46, 3603.
72. Kolb, A.; Huynh Dinh, T.; Igolen, J., J. Carbohydr. Nucleosides Nucleotides , 1975, 2, 37.
73. Jain, T. C.; Russell, A. F.; Moffatt, J. G., J. Org. Chem., 1973, 38, 3179.
74. Chu, C. K.; Reichman, U.; Watanabe, K. A.; Fox, J. J., J. Med. Chem., 1978, 21, 96.
75. Acton, E. M.; Fujiwara, A. N.; Goodman, L.; Henry, D. W., Carbohydr. Research, 1974, 33, 135.
76. Barnathan, G.; Huynh Dinh, T.; Kolb, A.; Igolen, G., Eur. J. Med. Chem., 1976, 11, 67.
77. Rosenthal, A.; Lee, H. H., J. Carbohydr. Nucleosides Nucleotides, 1978, 5, 559.
78. Stevens, J. D.; Fletcher, H. G. Jr., J. Org. Chem., 1968, 33, 1799.
79. Robins, R. K.; Townsend, L. B.; Cassidy, F.; Gerster, J. F.; Lewis, A.F.; Miller, R. L., Heterocycl. Chem., 1966, 3, 110. 80.
80. Tanaka, H.; Hayakawa, H.; Miyasaka, T., Chem. Pharm. Bull., 1982, 30, 1117.
81. Kalvoda, L.; Farkas, J.; Sorm, F., Tetrahedron Lett., 1970, 2297.
82. Buchanan, J. G.; Edgar, A. R.; Power, M. J.; Williams, G. C., J. C. S. Chem. Comm., 1975, 501.
83. Soto, T.; Watanabe, M.; Noyori, R., Tetrahedron Lett., 1978, 45, 4403.

84. Just, G.; Lim, M-I., Can. J. Chem., 1977, 55, 2993.

85. MacCoss, M.; Robins, M. J.; Rayner, B.; Imbach, J-L., Carbohydr. Res., 1977, 59, 575.

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