Carbon-13 NMR Spectra of *C*-Nucleosides. Showdomycin and β-Pseudouridine (1)

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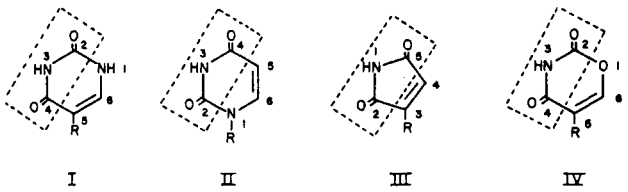
Sir:

Several pmr studies (3-6) on *C*-nucleosides have been published, however to date, there have been no reports on natural abundance carbon-13 magnetic resonance (cmr) spectra of *C*-nucleosides with the exception (7) of the cmr spectrum of Formycin B. Even this report (7) was incomplete as only two carbon atoms of the pyrazolo[4,3-*d*]-pyrimidine aglycon were assigned. We now wish to report on a study involving the cmr spectra of *C*-nucleosides related to uridine (IIa), a pyrimidine nucleoside.



I II III IV

a series, R = β-D-ribofuranose
b series, R = CH_3
c series, R = H

Figure 1

β-Pseudouridine (Ia, β-ψ) (8), Showdomycin (IIIa) (5), and Minimycin (IVa) (6) all fall into this classification of *C*-nucleosides which possess a striking structural similarity with uridine (IIa, Figure 1). These *C*-nucleosides differ from uridine in that they have a carbon-carbon linkage rather than a carbon-nitrogen linkage between the sugar moiety and heterocyclic aglycon. We have examined the cmr spectra of two of these *C*-nucleosides; β-Pseudouridine (Ia, β-ψ) and Showdomycin (IIIa).

The chemical shifts of β-ψ are presented in Table I along with the values (for comparison) for thymine (Ib) (9), uracil (Ic), uridine (IIa) and β-cyanuric acid riboside (β-CAR) (10). The ^{13}C chemical shifts shown for β-ψ were easily identified by means of off-resonance decoupling and comparison of the resonance positions with those in Ib and Ic. The only chemical shift differences worth noting in the spectrum of β-ψ are those for the carbons C5 and C6. The resonance positions for C5 and C6 are shifted 3.4 ppm and 2.4 ppm, respectively, to lower field as compared to Ib. These chemical shift changes are probably caused by complex electronic effects in changing from a methyl to ribose substituent.

The cmr chemical shifts for maleimide (IIIc), citraconimide (IIIb) (11), and showdomycin (IIIa) are included in Table I. In the case of IIIc, the differentiation between C2,5 and C3,4 based on off-resonance decoupling data is straightforward. The C3 carbon of IIIb is easily assigned from the expected 9-10 ppm downfield shift induced by methyl substitution (12). While C4 was predicted to move upfield 2-3 ppm based on a previous report (12), the actual shift was found to be somewhat larger (*ca.* 7 ppm). C2 and C5 exhibit only minor chemical shift perturbations in going from IIIc to IIIb and the assignments given in Table I have been confirmed by examination of the $^3J_{C\text{-}H}$ coupling constant for C2. It is interesting to note that for showdomycin (IIIa) the chemical shifts for C2 and C5 are accidentally degenerate. The chemical shifts for C3 and C4 are easily assigned by off-resonance decoupling and by comparing the spectra with that of IIIb. C3 is shifted to lower field (by *ca.* 3 ppm) as compared to IIIb and C4 is shifted an additional 0.7 ppm downfield. The trends noted for C3 and C4 in IIIc, IIIb, and IIIa are similar to those found at C5 and C6 in the series Ic, Ib, and Ia (Figure 2).

Recently, several pmr (4,13,14) studies have attempted to ascertain the glycosyl torsional angle (*syn* or *anti* conformation) in pyrimidine nucleosides on the basis of chemical shifts and coupling constants. The cmr data in Table I provide some interesting comparisons which may be pertinent to the question of conformational preference in solution. The chemical shifts for the ribose carbons in IIa and β-ψ exhibit certain variations when compared to those of β-CAR. While the variations at C5′ may be caused by the different exocyclic rotomeric conformations

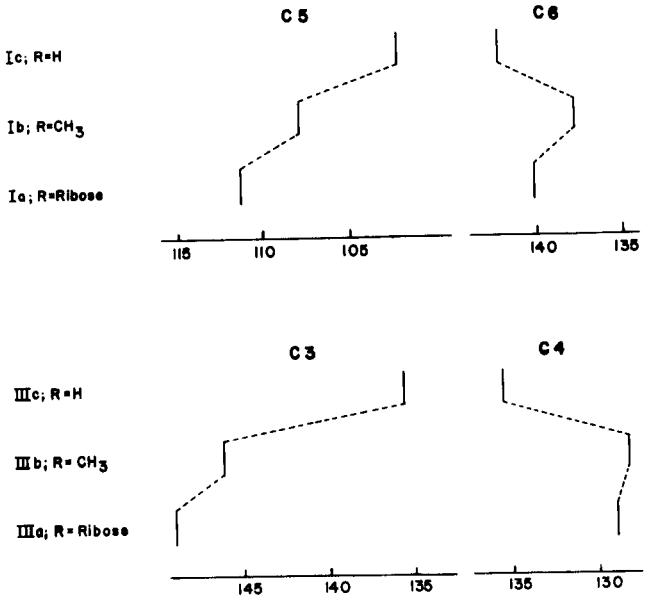


Figure 2. Specific chemical shifts for Ia-c and IIIa-c with respect to the TMS scale.

of the $-CH_2OH$ group (4), the shift variations at C4′ do not seem to follow a particular pattern and cannot be explained at this time. Only a minor variation in the cmr shifts at C3′ are observed whereas a 2.7 ppm range exists at C2′. An examination of a CPK molecular model of β-CAR indicates that the most logical conformation of the amphisbaenic aglycon would position *one* of the carbonyl functions near the C2′ of the ribose moiety. This steric perturbation undoubtedly contributes to the upfield shift for the resonance position of C2′ (15). Therefore, the observed downfield shift at C2′ for IIa and β-ψ as compared to the *amphisbaeno*-conformation of β-CAR, reflects a decrease of steric strain due to a preference for the *anti*-range. This rationale is consistent with the conclusions reached from the forementioned pmr studies (4,14).

It has been reported (16) that showdomycin in the crystalline state exists in the *syn*-conformation. However, due to the absence of other model riboside compounds for purposes of comparison, the cmr data (Table I) do not permit any conclusions with regard to the conformation of showdomycin in solution. The syntheses of nucleosides related to β-ψ and showdomycin which are essential to cmr spectral studies and the question of conformational changes in solution will be forthcoming from these laboratories.

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TABLE I

Carbon-13 Chemical Shifts (a) for β-Pseudouridine, Showdomycin, and Related Compounds

	Aglycon				Ribose					
Compound (°C) (b)	C2	C4	C5	C6	C1′	C2′ (c)	C3′ (c)	C4′	C5′	CCH_3
Ic; (40°)	151.54	164.41	100.34	142.16					61.13	
IIa; (37°)	151.03	163.49	102.01	141.00	88.03	73.81	70.14	85.09		
Ib; (37°)	152.37	164.99	107.85	137.76						11.87
Ia; (40°)	151.36	163.95	111.27	140.14	79.13	74.10	70.80	83.60	61.55	
β-CAR (d)	149.24	148.32		149.24	88.34	71.36	70.05	84.58	62.31	

Compound (°C) (b)	C2	C3	C4	C5	C1′	C2′	C3′	C4′	C5′	CCH_3
IIIc; (32°)	173.0	135.47	135.47	173.0						
IIIb; (32°)	173.24	146.11	128.17	172.30						10.35
IIIa; (38°)	171.87	148.94	128.91	171.87	77.52	75.01	70.76	83.60	61.19	

(a) All samples were dissolved in DMSO and run on a Varian XL-100/15 spectrometer equipped for Fourier transform operation. All chemical shifts were referenced to the internal DMSO line and then converted to the TMS scale using the formula $\delta TMS = \delta DMSO + 0.775 \times 10^{-2} T(°C) + 40.21$ ppm (M. T. Chenon and D. M. Grant, manuscript in preparation). (b) Sample temperature. (c) The C2′ and C3′ carbons were assigned according to H. H. Mantsch and I. C. P. Smith, *Biochem. Biophys. Res. Commun.*, 46, 808 (1972). (d) Reference 10; these values have been converted to the TMS scale.

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