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THE TAUTOMERIC STRUCTURE OF DEOXYCYTIDINE

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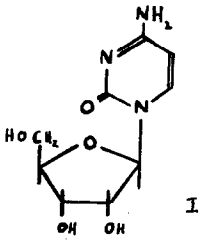
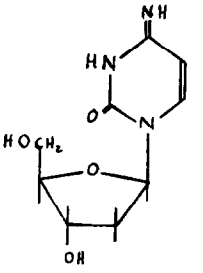
IN a recent paper on the n.m.r. spectra of various nucleosides[1], it was proposed that, whereas cytidine exists in the amino form (I), 2'-deoxycytidine exists in the imino form (II). No explanation was offered for this profound difference, though far-reaching conclusions regarding the hydrogen bonding in nucleic acids were drawn. We have reinvestigated this problem and found that the results of Gatlin and Davis[1] are incorrect. In fact, both cytidine and 2'-deoxycytidine have the amino form, as expected from numerous studies on tautomerism in aminopyrimidines[2], and from Angell's study of the infrared spectra of these nucleosides[3].



I



II

[1] L. Gatlin and J.C. Davis, Jr., J. Amer. Chem. Soc. 84, 4464 (1962).

[2] T.L.V. Ulbricht, "Chemistry of Nucleic Acid Bases and Nucleosides", in "Comprehensive Biochemistry", ed. by M. Florkin and H. Stotz, vol. 8, Elsevier, in press.

[3] C.L. Angell, J. Chem. Soc. 504 (1961).

Gatlin and Davis used two different salts, cytidine hemisulphate and deoxycytidine hydrochloride, in their studies. In the present work we have measured the n.m.r. spectra of cytidine, deoxycytidine and 1-methyldeoxycytidine (which must have the imino form, III) both as free bases and as hydrochlorides. (1-Methyldeoxycytidine, which has not previously been reported, was isolated as the methosulphate, m.p. 146°, by methylation of II with dimethyl sulphate). The solvent, dimethyl sulphoxide, was dried by azeotropic distillation with benzene, and twice distilled in vacuo, using a vigreaux column (some decomposition occurs on distillation at atmospheric pressure). The free bases and their hydrochlorides were dried in vacuo at 110° and 90° respectively. N.m.r. spectra were obtained with a varian A-60 spectrometer[4], and chemical shifts are given in p.p.m. relative to the aromatic peak of toluene as internal reference.

In this paper we are concerned only with the N-H peaks. The chemical shifts are reported in Table 1.

TABLE 1.

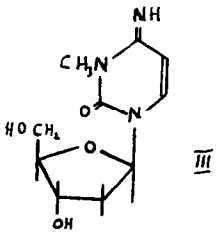
Chemical Shifts of Cytosine Nucleosides

Nucleoside	N-H Peaks	Number of Protons
Cytidine	-0.08	2
Deoxycytidine	0	2
1-Methyldeoxycytidine	Not identified	
Cytidine. HCl	-1.63, -2.77	1 each
Deoxycytidine. HCl	-1.59, -2.70	1 each
1-Methyldeoxycytidine. HCl	-2.32, -3.46	1 each

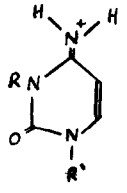
[4] These spectra were run at Imperial College, by kind permission of Prof. D.H.R. Barton, F.R.S.

It is evident that the spectra of the free bases, cytidine and deoxycytidine, are very similar to each other, and quite different from those of the hydrochlorides, which are also similar to each other. Comparison of these results with those of Gatlin and Davis reveals that the spectrum they report for cytidine is that of the free base, whereas their spectrum of deoxycytidine is that of the hydrochloride. Their erroneous conclusions were based on the difference between these two spectra.

We have identified only two protons, not three, in the spectra of the hydrochlorides. The most probable structure of the cation in these compounds is IV (R=H), and we suggest that the N-H peaks in the hydrochlorides are those of the $=N^{+}H_2$ protons. This is confirmed by the similarity of the spectrum of the hydrochloride of 1-methyldeoxycytidine (IV, R=CH_3).



III



R' = ribose, 2-deoxyribose

We have also examined the infrared spectra of cytidine and deoxycytidine (free bases), and as Table 2 shows, our results confirm those of Angell and differ from those of Gatlin and Davis.

TABLE 2.

Infrared Spectra of Cytosine Nucleosides (Nujol)

Nucleoside	N-H Frequencies, cm^{-1}	Reference
Cytidine	broad band, 3200-3400	1
	3225 and 3333	3
	3200 and 3330	Present study
Deoxycytidine	3350 and 3405	1
	3106 and 3370	3
	3120 and 3350	Present study

All the evidence from n.m.r. and infrared spectra is consistent with the view that both cytidine and deoxycytidine have the amino form.