Third International Electronic Conference on Synthetic Organic Chemistry (ECSOC-3), www.mdpi.org/ecsoc-3.htm, September 1-30, 1999

[A0033]

Base-Pairing Studies of a Ring-Expanded ("Fat") Nucleoside Analogue Possessing Potent Antiviral Activity

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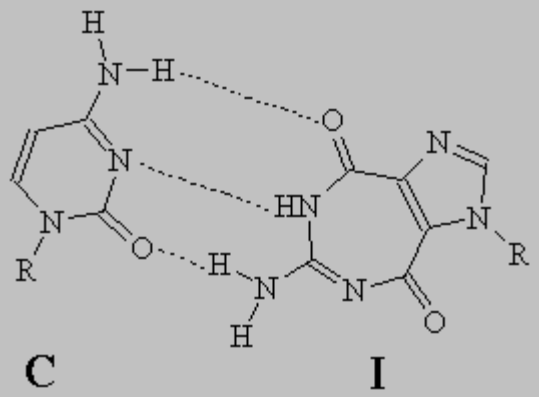
Received: 20 August 1999 / Uploaded: 23 August 1999

Keywords: ^{1}H NMR Studies, Base-Pairing Properties, Ring-Expanded ("Fat" Nucleoside

Ring-expanded ("fat") nucleosides and nucleotides are potentially useful probes for nucleic acid metabolism, structure, and function. With their structural resemblance to natural purines, they are a rich source of substrates or inhibitors of enzymes of nucleic acid metabolism as well as of those requiring energy cofactors such as ATP or GTP. As ring-expansion is anticipated to considerably affect the electronic, spatial, and geometric characteristics, they are also excellent probes for steric and conformational constraints of nucleic acid double-helices.

The ring-expanded nucleoside **I** that we recently synthesized showed potent anti-hepatitis B virus activity *in vitro* in submicromolar range with practically no toxicity even up to tens of thousands of times the therapeutic concentration levels. As part of a program to explore the mechanism of biological activity of **I**, it became necessary to investigate the base-pairing properties of **I** with appropriate pyrimidine partners. Since **I** can exist in several tautomeric forms in solution, it is theoretically capable of base-pairing with either cytidine (C) or Uridine (U). We present here the results of our extensive ^{1}H NMR studies, which suggest that **I** base-pairs strongly with C, but not with U. These results further imply that the predominant tautomeric form of **I** is amino-diketo form as depicted below.



C **I**

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