STRUCTUAL EFFECTS OF CYTIDINE $2'$ RIBOSE MODIFICATIONS AS DETERMINED BY IRMPD ACTION SPECTROSCOPY

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Modified nucleosides, both naturally occurring and synthetic play an important role in understanding and manipulating RNA and DNA. Naturally occurring modified nucleosides are commonly found in functionally important regions of RNA and also affect antibiotic resistance or sensitivity. Synthetic modifications of nucleosides such as fluorinated and arabinosyl nucleosides have found uses as anti-virals and chemotherapy agents. Understanding the effect that modifications have on structure and glycosidic bond stability may lend insight into the functions of these modified nucleosides.

Modifications such as the naturally occurring $2'$-O-methylation and the synthetic $2'$-fluorination are believed to help stabilize the nucleoside through the glycosidic bond stability and intramolecular hydrogen bonding. Changing the sugar from ribose to arabinose alters the stereochemistry at the $2'$ position and thus shifts the 3D orientation of the $2'$-hydroxyl group, which also affects intramolecular hydrogen bonding and glycosidic bond stability. The structures of $2'$-deoxy-$2'$-fluorocytidine, $2'$-O-methylcytidine and cytosine arabinoside are examined in the current work by measuring the infrared spectra in the IR fingerprint region using infrared multiple photon dissociation (IRMPD) action spectroscopy. The structures accessed in the experiments were determined via comparison of the measured IRMPD action spectra to the theoretical linear IR spectra determined by density functional theory and molecular modeling for the stable low-energy structures. Although glycosidic bond stability cannot be quantitatively determined from this data, complementary TCID studies will establish the effect of these modifications. Comparison of these modified nucleosides with their RNA and DNA analogues will help elucidate differences in their intrinsic chemistry.