

P028 Synthesis and Structure of Modified and ^{15}N -Enriched Pseudouridine RNAs

Christine S. Chow, Jean-Paul Desaulniers, Yu-Cheng Chang

Department of Chemistry, Wayne State University, Detroit, MI 48202 USA

Pseudouridine is the most abundant modified nucleoside found in nature. This C-glycoside and its variants are found in many types of ribonucleic acids including ribosomal RNAs (rRNAs). The synthesis of pseudouridine and its derivatives with ^{15}N at specific sites will allow for NMR studies to be carried out. Such studies are important in order to better understand the structure and dynamics of modified rRNAs, such as helix 69 in the large subunit rRNA. We have completed the synthesis of $[3-^{15}\text{N}]$ pseudouridine using a selective deprotection strategy, and carried out the synthesis of $[1,3-^{15}\text{N}]$ pseudouridine by coupling 5-iodo-2,4- $[1,3-^{15}\text{N}]$ dimethoxypyrimidine to a protected gamma lactone. Reduction, ring-closing, and deprotection reactions lead to the final ^{15}N -enriched pseudouridine product. Several of the intermediates in the synthesis can be used to generate 1-methylpseudouridine and 1-methyl-3-(3-amino-3-carboxypropyl)pseudouridine. Using phosphoramidite chemistry, the modified pseudouridines are then incorporated site-specifically into a variety of RNAs and used for biophysical (circular dichroism and UV melting) and NMR structure studies, as well as structure probing studies with transition metal complexes.