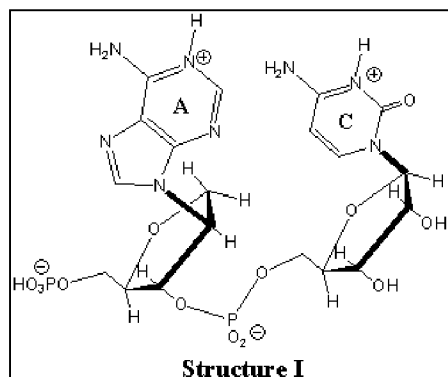


**Structural Investigation of a Non-natural Dinucleotide with anti-HIV Integrase Activity.** M. Gary Newton<sup>1</sup>, Charles F. Campana<sup>4</sup>, Guochen Chi<sup>2</sup>, Doowon Lee<sup>1</sup>, Z.-J. Liu<sup>1</sup>, Vasu Nair<sup>2</sup>, James Phillips<sup>3</sup>, John P. Rose<sup>1</sup>, B.-C. Wang<sup>1</sup>, Depts. of <sup>1</sup>Biochemistry & Molecular Biology, <sup>2</sup>Pharmaceutical & Biomedical Sciences, Univ. of Georgia, Athens, GA 30602; <sup>3</sup>Duke Univ. Medical Center, Durham, NC 27710; <sup>4</sup> Bruker AXS Inc., Madison, WI 53711.

HIV-1 integrase incorporates double-helical HIV DNA into host chromosomal DNA. Some small oligodeoxynucleotides of natural origin are capable of interfering with HIV integrase by competing with the viral DNA but these “natural” oligonucleotides are rapidly cleaved by nucleases. Non-natural dinucleotides, with unusual internucleotide phosphate bonds, have been designed and synthesized that exhibit 5'- and 3'-exonuclease stability and anti-HIV integrase activity. We now describe the single-crystal X-ray structure of one of these non-natural dinucleotide 5'-phosphates: pIsodApC (**Structure I**).



Needle crystals (0.15x0.15x0.35mm) of pIsodApC (**I**) were mounted on a BRUKER SMART 6000 detector system. X-ray data were measured using CuK $\alpha$  radiation. In all, merging the 23451 measured reflections yielded 5272 unique X-ray data. Cell dimensions: a=b=12.566Å, c=38.708Å, space group: P4<sub>1</sub>2<sub>1</sub>2 (#92). The structure was solved (by direct methods) and refined using both TEXSAN and SHELXTL program suites. The asymmetric unit contained C<sub>19</sub>H<sub>25</sub>N<sub>8</sub>O<sub>13</sub>P<sub>2</sub>· 6\_H<sub>2</sub>O. The final R was 4.3%.

Details of the structure and comparisons to some previously determined natural dinucleotides will be reported.