SINGLE CONFORMATION SPECTROSCOPY OF SUBEROYLANILIDE HYDROXAMIC ACID: A MOLECULE BITES ITS TAIL

DI ZHANG, JACOB DEAN and TIMOTHY S. ZWIER, *Department of chemistry, Purdue University, West Lafayette, IN 47906..*

Suberoylanilide hydroxamic acid ($C_6H_5NHCO(CH_2)_6CONHOH$, SAHA) is a histone deacetylase inhibitor approved by the FDA for the treatment of cutaneous T-cell lymphoma. With one hydrogen bonding group adjacent to ring and the other at the end of a long C_6 hydrocarbon tail, SAHA possesses an interesting potential energy landscape to be probed by single-conformation methods. A large number of extended structures favored by entropy are offset by a few structures in which head-to-tail or tail-to-head H-bonds close a large loop between the two groups separated by the C_6 chain. We use laser desorption to bring SAHA into the gas phase and cool it in a supersonic expansion before interrogation with resonant two-photon ionization. Single-conformation UV spectra in the S_0-S_1 region and infrared spectra in the hydride stretch region were recorded using IR-UV hole-burning and resonant ion-dip infrared (RIDIR) spectroscopies, respectively. Four different conformers were observed and spectroscopically characterized. Comparison of the experimental IR spectra with density functional theory (DFT) calculations leads to assignments for two of the major conformers, which adopt head-to-tail and tail-to-head binding patterns. The implication of the observed structures for the folding landscape and configuration preference of SAHA will be discussed.