DETERMINATION OF THE ABSOLUTE CONFIGURATION AND ENANTIOMERIC EXCESS OF MOLECULES THAT ARE CHIRAL BY VIRTUE OF DEUTERIUM SUBSTITUTION USING MOLECULAR ROTATIONAL SPECTROSCOPY

ZOUA PA VANG, MITCHELL D MILLS, JOSEPH R CLARK, *Department of Chemistry, Marquette University, Milwaukee, WI, USA*; JUSTIN L. NEILL, REILLY E. SONSTROM, *BrightSpec Labs, BrightSpec, Inc., Charlottesville, VA, USA*; KEVIN J MAYER, CHANNING WEST, MARTIN S. HOLDREN, *Department of Chemistry, The University of Virginia, Charlottesville, VA, USA*; HALEY N. SCOLATI, *Department of Chemistry, University of Virginia, Charlottesville, VA, USA*; BROOKS PATE, *Department of Chemistry, The University of Virginia, Charlottesville, VA, USA*.

New techniques for chiral analysis have recently emerged from the field of rotational spectroscopy. Traditional approaches to chiroptical spectroscopy, like circular dichroism, produce chiral signatures that are too weak for practical applications in rotational spectroscopy. The introduction of microwave three-wave mixing spectroscopy by Patterson, Schnell, and Doyle in 2013 renewed interest in chiral analysis by rotational spectroscopy. Work in the field has included the development of a chiral derivatization method that uses noncovalent interactions to generate complexes between the analyte and a small, chiral "tag" molecule in the pulsed jet expansion used in many Fourier transform microwave spectroscopy instruments. Recently, there has been increasing interest in using deuterium incorporation to improve the safety and efficacy of active pharmaceutical ingredients (APIs). The most chemically specific modification of the API needed to achieve improved drug performance can potentially involve the incorporation of a single deuterium atom at a prochiral R_1-CH_2-R_2 position. Applications of rotational spectroscopy approaches to chiral analysis will be discussed in the context of aiding the development of catalytic methods to add a single deuterium at the enzyme targeted benzylic CH_2 position. The relative strengths and weaknesses of three-wave mixing and chiral tag rotational spectroscopy in meeting the needs of rapid analysis of the enantioisotopomers produced using this new chemistry will be discussed.