DETERMINATION OF ABSOLUTE CONFIGURATION IN CEDROL USING CHIRAL TAG ROTATIONAL SPECTROSCOPY

LUCA EVANGELISTI, *Dipartimento di Chimica G. Ciamician, Università di Bologna, Bologna, Italy*; BROOKS PATE, TAYLOR SMART, CHANNING WEST, MARTIN S. HOLDREN, KEVIN J MAYER, *Department of Chemistry, The University of Virginia, Charlottesville, VA, USA*.

Rotational spectroscopy has been extended for use in chiral analysis by both the chiral tagging and three-wave mixing methods. The chiral tagging method uses complex formation between two species in a pulsed jet: the first, a small chiral tag of known absolute configuration and the second, an unknown analyte. The complexing of the tag with the unknown analyte converts the enantiomers to diastereomers. Cedrol ((1S,2R,5S,7R,8R)-2,6,6,8-tetramethyltricyclo[5.3.1.$0^{1,5}$]undecan-8-ol, $C_{16}H_{26}O$, MW 222.37) was chosen as a test molecule for the chiral tagging method to assess the potential for extending the approach to larger molecules. In addition to its large size, cedrol has conformational flexibility from both the internal rotation of the hydroxyl group and a ring pucker coordinate. As the analyte molecules become larger, there is the potential that the difference in the rotational constants of the diastereomer complexes differ by amounts too small to reliably predict by quantum chemistry making difficult to produce a high-confidence assignment of the absolute configuration. The chiral tag measurement of cedrol used propylene oxide as the tag. The estimates of the rotational constants and dipole moments of the complexes were obtained using the B3LYP-D3BJ method and def2TZVP basis set. Six isomers for the cedrol / propylene oxide complex were observed using an enantiopure tag. The challenges in identifying these isomers in the quantum chemistry calculations will be discussed. The agreement between the experimental and theoretical rotational constants was at the $\sim$1% level and this makes it possible to assign the absolute configuration. The quality of the theoretical structure of the cedrol / propylene oxide complex was assessed by determining the experimental carbon atom framework geometry through 13C isotopic substitution using natural abundance.