

ENANTIOMERIC EXCESS MEASUREMENTS OF ISOPULEGOL USING CHIRAL TAG SPECTROSCOPY

KEVIN J MAYER, CAITLIN EMBLY, BROOKS PATE, *Department of Chemistry, The University of Virginia, Charlottesville, VA, USA*; LUCA EVANGELISTI, *Dipartimento di Chimica G. Ciamician, Università di Bologna, Bologna, Italy*.

Chiral analysis was performed on samples of isopulegol and its isomers using chiral tag rotational spectroscopy. Isopulegol, with three chiral centers, has 8 stereoisomers. There are four diastereomers with distinct geometries and the diastereomer ratio can be determined using traditional rotational spectroscopy. To determine the enantiomeric ratio for each diastereomer the chiral tagging method was used to convert these enantiomers into distinguishable diastereomer complexes. Isopulegol was placed into the nozzles of a chirped-pulsed Fourier transform microwave spectrometer and was heated to 323K. The isopulegol was complexed with a 0.1% mixture of propylene oxide in neon as the carrier gas. The measurement methodology for EE determinations is: 1) a 400K average spectrum is measured using the enantiopure S-propylene oxide, 2) the tag is purged by flowing pure neon over the sample and heating, and 3) a 400K average spectrum using racemic propylene oxide is measured. Enantiopure samples of (-)-isopulegol and (+)-isopulegol were purchased from Sigma Aldrich and used to create standards of 0, 5, 10, 30, 55, 80, and 90 enantiomeric excess of (-)-isopulegol. The calibration curve was fit using a linear expression with zero offset giving a slope of 1.005 ± 0.007 ($R^2 = 0.99935$). These results demonstrate that the method has linear performance over the full EE scale. The reference solution with EE=80 was measured in six separate runs to assess reproducibility. The average of the measurements was 80.595% with a standard deviation of 0.274. A sample of isopulegol provided as a mixture of isomers (Alfa Aesar) was analyzed using the chiral tag method. The enantiomeric excess for the two most abundant diastereomers were determined: isopulegol: EE=4.1(4) and neo-isopulegol: EE=4.8(4). The similar enantiomeric excess values for these isomers is consistent with the usual production method for isopulegol where the EE of the reagent (citronellal) sets the EE for all four diastereomer products.