

DETERMINATION OF ENANTIOMERIC EXCESS IN THE HIGH ENANTIOPURITY LIMIT USING CHIRAL TAGGING ROTATIONAL SPECTROSCOPY

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Chiral tag rotational spectroscopy can be used for quantitative determination of the ratio of the two enantiomers of a chiral molecule. The strategy for chiral tag rotational spectroscopy is to convert the enantiomers of the analyte into diastereomers through non-covalent attachment of a small, chiral tag molecule. The analyte enantiomer ratio, which is used to determine the enantiomeric excess (EE), is determined by comparing the transition intensities of rotational transitions for the homochiral and heterochiral complexes when both a racemic and enantiopure tag sample is used. A calibration curve for EE determination of 3-methylcyclohexanone tagged with 3-butyn-2-ol will be presented. The role that intensity fluctuations in back-to-back measurements of the rotational spectra of the chiral tag complexes play in determining the EE measurement accuracy will be described. In applications to pharmaceutical chemistry the main need is the ability make quantitative EE determinations in the high enantiopurity limit of the analyte. This requirement poses challenges for chiral tag rotational spectroscopy from both the measurement sensitivity and the availability of high enantiopurity tag samples. Two analysis methods for high EE measurements will be discussed. In one case, the enantioimpurity detection limit is decreased by the co-adding of multiple rotational transitions of the homochiral and heterochiral tag complex. The second strategy uses a lower enantioimpurity tag to speed the EE determination of high enantioimpurity samples. In this case, the ability to accurately determine the tag EE is crucial and the functional dependence of EE measurement precision in chiral tag rotational spectroscopy provides the limit on measurement accuracy that can be achieved.