Landmark research publication in JACS: A complete solution for site-specific deuteration

Copper-Catalyzed Transfer Hydrodeuteration of Aryl Alkenes with Quantitative Isotopomer Purity Analysis by Molecular Rotational Resonance Spectroscopy

Zoua Pa Vang, Albert Reyes, Reilly E. Sonstrom, Martin S. Holdren, Samantha E. Sloane, Isabella Y. Alansari, Justin L. Neill, Brooks H. Pate, and Joseph R. Clark

J. Am. Chem. Soc., 2021, https://doi.org/10.1021/jacs.1c00884

"We anticipate that the advances reported for the selective hydrodeuteration chemistry and MRR spectroscopy will facilitate new reaction discovery in selective deuteration chemistry and expand the utility of deuterium-labeled organic compounds in applications that require the molecule has high deuterium content at precisely the desired site."

Prof. Joe Clark
Marquette University

The Clark research group works on developing new catalytic methods for the precise installation of deuterium into small organic molecules. Dr. Clark received his B.S. in chemistry from St. John Fisher College, his Ph.D. from the University at Buffalo, with Professor Steven T. Diver, and worked as a NIH Ruth Kirschstein Postdoctoral Fellow under the direction of Professor M. Christina White at UIUC.

A Powerful Combination of Catalysis and Spectroscopy

Deuteration has long held the promise of improving drug stability and reducing toxicity, among other benefits. Until now, a general method to install deuterium into a small molecule in a highly selective manner was unavailable. In the JACS article, Prof. Clark details novel chemistry that allows for site-specific deuteration to access deuterated small molecules with high levels of isotopic purity.

To characterize the unique chemistry developed by the Clark Group, Molecular Rotational Resonance (MRR) spectroscopy was used to identify and quantify all isotopic variants. BrightSpec's MRR technology is the only analytical technique that can practically measure site-specific deuteration, an area where NMR falls short. The article states the following key features of MRR for their solution:

No Reference Standards Required

Isotopomers and isotopologues have distinct MRR spectra that can be predicted to high accuracy using the theoretical equilibrium geometry from quantum chemistry. This feature makes it possible to identify both the isotopomers and isotopologueswith high confidence without the need for reference samples.

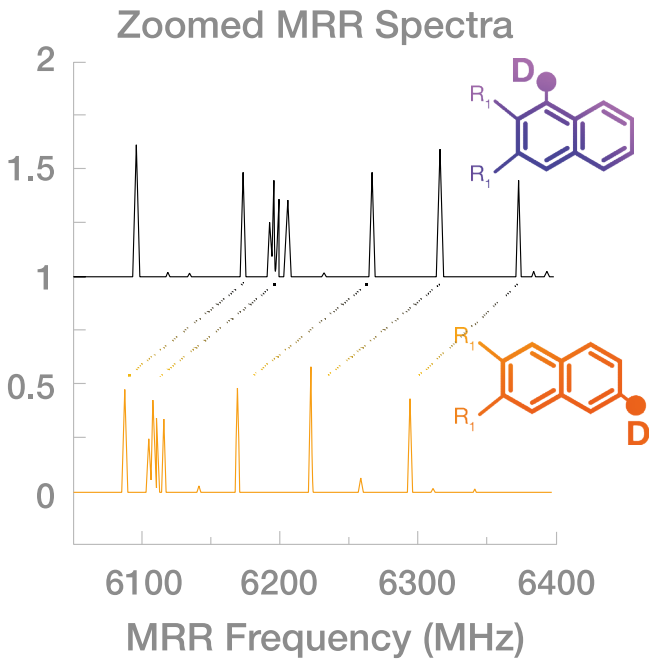
Analyze Mixtures Directly

MRR instruments provide high spectral resolution so that isotopologue and isotopomer mixtures can be quantitatively analyzed without issues arising from signal overlap.

High-throughput Analysis

Rapid analysis is achieved using the isoMRR making it possible to screen a wide range of reaction conditions for isotopic reactions and optimizing the reaction process.

isoMRR



MRR of Deuterated Isotopmers

Moving the position of a deuterium on a drug candidate creates an isotopmer. MRR spectroscopy provides unique spectra for each isotopic species as shown above. It removes any ambiguity when analyzing isotopic product mixtures consisting of isotopologues and isotopomers that share deuterium substitution at the same atom such that several isotopic species contribute to the same $^{1}H/^{2}H$ resonance in an NMR spectrum. High-throughput, targeted analysis is possible using the isoMRR instrument with about 3 mg of sample and 20-minute measurement time.

To lean more, please contact:
Walter Colsman, CEO
Email: water.colsman@brightspec.com

BrightSpec, Inc.
770 Harris Street Suite 104b
Charlottesville, Virginia 22903

BrightSpec