

University of Massachusetts Medical School

eScholarship@UMMS

UMass Center for Clinical and Translational
Science Research Retreat

2017 UMass Center for Clinical and
Translational Science Research Retreat

May 16th, 1:45 PM


Selective Environmentally Benign Synthesis of Isotope Labeled Compounds: Introduction of Deuterium into Compounds of Medicinal Relevance

Anne Kokel
University of Massachusetts Boston

Et al.

Let us know how access to this document benefits you.

Follow this and additional works at: https://escholarship.umassmed.edu/cts_retreat

 Part of the [Chemistry Commons](#), and the [Translational Medical Research Commons](#)

Kokel A, Kadish D, Torok B. (2017). Selective Environmentally Benign Synthesis of Isotope Labeled Compounds: Introduction of Deuterium into Compounds of Medicinal Relevance. UMass Center for Clinical and Translational Science Research Retreat. Retrieved from https://escholarship.umassmed.edu/cts_retreat/2017/posters/42

Creative Commons License



This work is licensed under a [Creative Commons Attribution-Noncommercial-Share Alike 3.0 License](#). This material is brought to you by eScholarship@UMMS. It has been accepted for inclusion in UMass Center for Clinical and Translational Science Research Retreat by an authorized administrator of eScholarship@UMMS. For more information, please contact Lisa.Palmer@umassmed.edu.

SELECTIVE ENVIRONMENTALLY BENIGN SYNTHESIS OF ISOTOPE LABELED COMPOUNDS: INTRODUCTION OF DEUTERIUM INTO COMPOUNDS OF MEDICINAL RELEVANCE

Anne Kokel, Dora Kadish, Béla Török
Department of Chemistry, University of Massachusetts Boston

Deuterium (^2H) is a less abundant isotope of hydrogen that possesses an additional neutron resulting in significant differences in the properties of a ^1H -containing-molecule compared to its ^2H homologues. Deuterium labeled organic compounds are valuable in medicinal chemistry as they offer widespread applications. For instance, in imaging deuterium labeling can serve as biological tracers, thus, deuterated drugs can provide better understanding of the metabolic pathways; they can also help localize the metabolites of the drug and assess their toxicity. While metabolic enzymes easily transform drug molecules to metabolites that the body can excrete, the introduction of deuterium to drugs appears to strengthen the resistance of drugs toward metabolism. In fact, the carbon-deuterium bond is known to be six to ten times stronger than its C- ^1H counterpart. The higher the stability, the longer the drug remains intact, which allows lower dosage, potentially causing fewer side effects. Due to the carbon-deuterium bond strength, deuterated drugs can also prevent the formation of toxic metabolites observed with its hydrogen-containing homologue.

There are several known methods for the introduction of deuterium to organic compounds; most methods, however, do not conform to the recent expectations and standards of sustainable synthesis. Therefore, a green synthesis of deuterated organic compounds would be an important advance in producing these compounds in an environmentally sustainable way. Thus, we have turned our attention to the Al- H_2O system that is commonly applied for hydrogenation reactions. Replacing the H_2O with its deuterated version D_2O in the system constitutes an easy, economic and safe source of deuterium. The application of either the commercially available Ni-Al alloy or Al in combination with Pd, a common hydrogenation catalyst, for the H-D exchange of compounds with reactive C-H bonds was performed, while yielding no harmful byproducts. The low reactivity of the aluminum metal was significantly enhanced by the application of ultrasonic irradiation prior to the reaction. The H-D exchange reaction was carried out under microwave irradiation and achieved good yields in no more than 1h. The success of the method was demonstrated by applying a broad variety of compounds from essential amino acids to actual drug compounds.

Contact:

Anne Kokel
University of Massachusetts Boston
Anne.Kokel001@umb.edu