

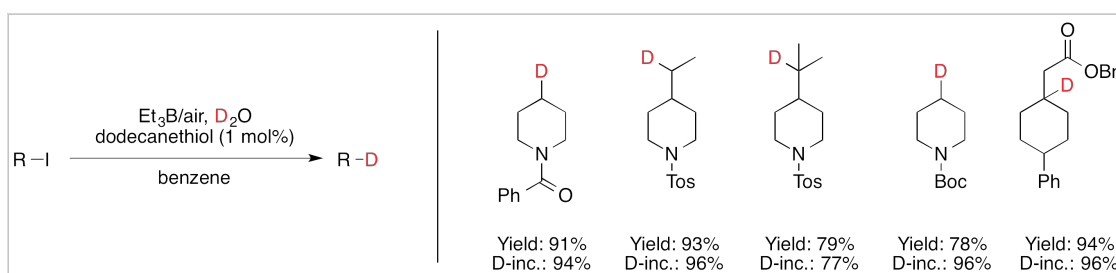
## Radical Deuteration of Alkyl Iodides Catalyzed by Thiol and Mechanistic Studies on Deoxygenation Reactions of Xanthates

V. Soulard<sup>1</sup>, G. Villa<sup>1</sup>, D. Vollmar<sup>1</sup>, P. Renaud<sup>1\*</sup>

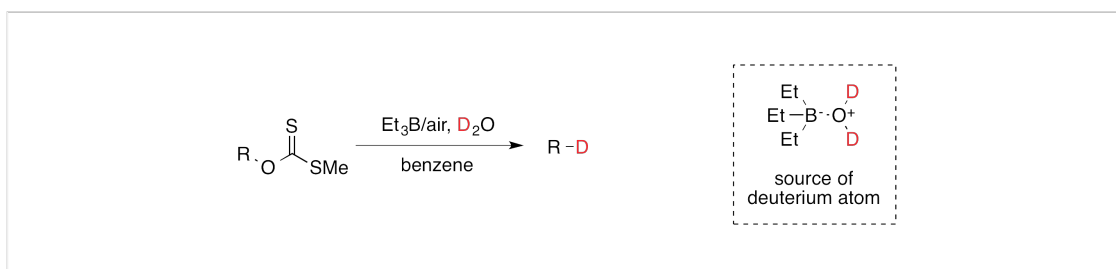
<sup>1</sup>University of Bern

Recently, there has been a growing interest in the pharmaceutical industries to incorporate deuterium in drugs candidates to improve their metabolism and pharmacokinetic properties<sup>1</sup>. A significant number of deuterated drug candidates (heavy drugs) have been synthesized and forwarded to clinical trials, such as Deutetrabenazine (Austedo®, TEVA pharmaceuticals) which is the first deuterated drug on the market. However, preparation of organic compounds selectively labelled with deuterium atom, remains a challenging synthetic problem. Radical deuteration of alkyl halides is one of the most efficient approach to perform this task. It is usually run using organotin deuterides<sup>2</sup> but this method has three major drawbacks: organotin deuterides are expensive, toxic<sup>3</sup> and led to product contamination.

We report here a method to deuterate alkyl iodides via a radical pathway with deuterated water as source of deuterium atom. Triethylborane is used to initiate and propagate the chain and dodecanethiol is used as a catalyst<sup>4</sup>. High deuterations and yields are obtained using this method which is compatible with a large range of functional groups.



The development of the deuteration method led us to discoveries that incite us to reinvestigate the mechanism of xanthates deoxygenation described by Wood *et al.*<sup>5</sup> (see below) who used heavy water activated by trialkylboranes as a source of deuterium atom.



[1] Mullard, A. *Nat. Rev. Drug Discovery* **2016**, 15, 219.

[2] Curran, D. P.; Ramamoorthy, P. S. *Tetrahedron* **1993**, 49 (22), 4841–4858.

[3] I. J. Boyer, *Toxicology* **1989**, 55, 253–298.

[4] B. M. Mikhailov; Y. N. Bubnov *Zh. Obshch. Khim.* **1961**, 31, 160-166.

[5] D. A. Spiegel, K. B. Wiberg, L. N. Schacherer, M. R. Medeiros, J. L. Wood, *J. Am. Chem. Soc.* **2005**, 127, 12513–12515.