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Short Research Article

Convenient and efficient tritiation of aristolochic acid I (AAI) and aristolochic acid II (AAII) with tritiated water[†]

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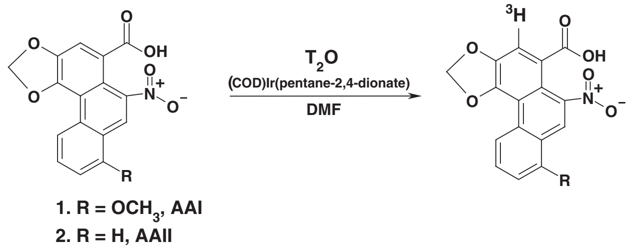
Abstract: Iridium-catalysed isotope exchange with tritiated water is an efficient way to introduce tritium into polar molecules. The method is feasible for compounds containing a nitro group.It has been confirmed through our experiment that using excess tritiated water, the H/T exchange can be quantitative.

Keywords: tritiation; tritiated water; aristolochic acid

Introduction

It has been discovered by Lockley *et al.* [1], that aromatic compounds bearing an *ortho*-directing substituent may be deuterated by exchange with deuterium oxide in the presence of a range of cycloocta-1,5-dienyliridium (I)2,3-dionate catalysts. The exchange takes place in several dipolar aprotic solvents and is directly applicable to the deuteration of polar compounds. Isotope incorporation is efficient and regiospecific. The method is applicable to a wide range of ortho-directing groups some of which are only weak directors for alternative ortho-labeling approaches.



1. R = OCH_3, AAI
2. R = H, AAII

Results and discussion

Direct tritiation by tritium gas exchange using iridium catalyst is a commonly used technique. However, this method requires the compounds are soluble in non-polar solvents (like CH_2Cl_2). This excludes many polar and ionic compounds of interest. It also limits the presence of nitro group since it is prone to reduction.

Lockley has screened a series of metal derivatives and found the most active catalyst to be 1, 5 cyclooctadienyl iridium (I) pentane-2,4-dionate. This is a commercially available compound with excellent stability and solubility properties.

In our experiment we added iridium catalyst and T_2O(sp. act. 50 Ci/ml) in DMF to a solution of aristolochic acid in DMF. The reaction was heated at 95°C for 4 h. TLC analysis indicated the incorporation of tritium in the compound. The reaction was then worked up and purified by Prep HPLC.

We have proposed the following mechanism:

(1) COD is replaced by solvent molecules to form the real catalyst.
(2) Iridium is inserted into C–H bond (oxidative addition).
(3) Subsequent coordination to T_2O, followed by H/T exchange.
(4) Final reductive elimination releasing tritiated product.

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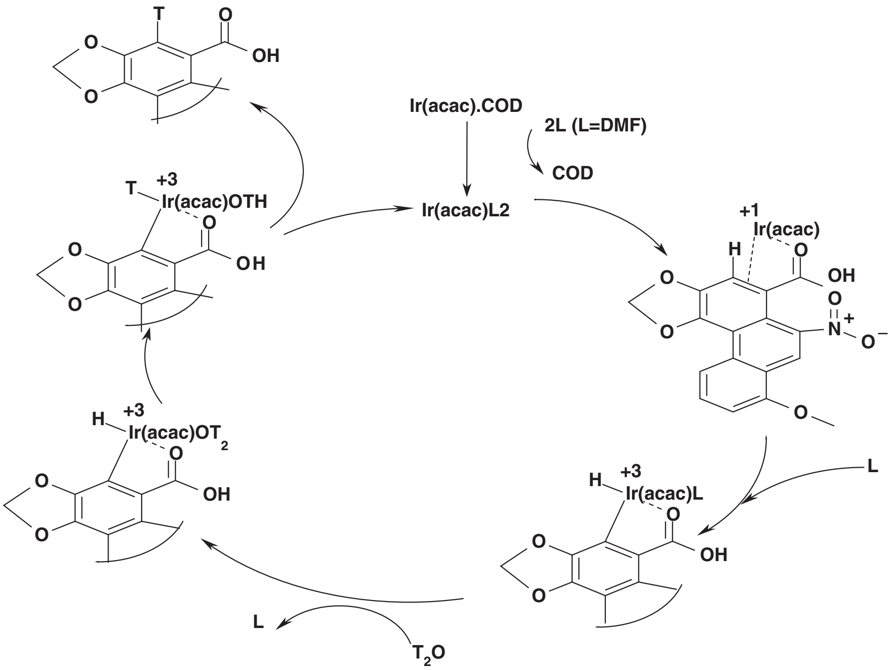

The specific activities for both AAI and AAII are determined by LC/MS combined with liquid scintillation counting, at about 0.4 Ci/mmol. Meaning there are about 100% tritium incorporation compared to the tritiated water used.

REFERENCE

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