ACS Medicinal Chemistry Letters

In This Issue

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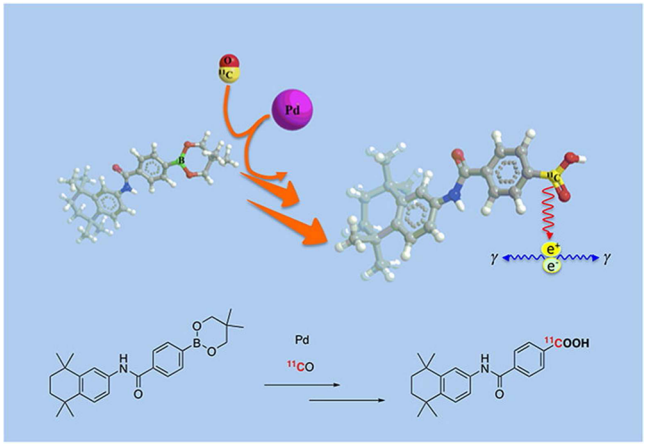
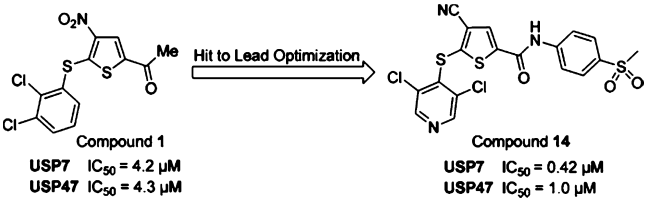
A MORE EFFICIENT RADIOSYNTHESIS TECHNIQUE



Current imaging technologies tremendously aid in the clinical diagnosis of cardiovascular disease, cancer, and neurodegenerative diseases, among others. Positron emission tomography is ideal for clinical imaging due to its high sensitivity and noninvasiveness. However, this technique relies on radiolabeled probes with short-lived positron-emitting radionuclides, such as ^{11}C-radiolabeled probes. Thus, radiosynthesis of carbon-11 compounds with improved radiochemical yield and shortened reaction time is highly desirable.

In this issue, Takashima-Hirano et al. (DOI: 10.1021/ml300160w) improved upon the current [^{11}C] carbonylation technique that requires high-pressure and microfluidic systems. The authors were able to synthesize carbon-11 esters in a rapid and efficient manner under mild conditions. This technique could be applied to a variety of [^{11}C] synthesis of biologically important esters and carboxylic acids, which could expand the current array of diagnostic imaging tools.

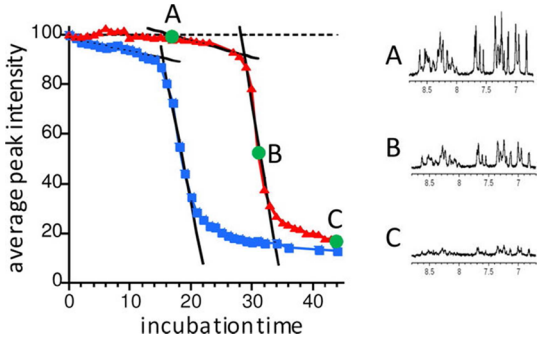
DUAL INHIBITORS OF DEUBIQUITINATING ENZYMES



Ubiquitin is a highly conserved small protein and a key player in the regulation of select protein contents in the cell. It is involved in the degradation pathway by covalently binding to regulatory proteins, which then triggers a series of cellular processes such as endocytosis, signal transduction, and transcriptional regulation. Deubiquitinating enzymes act to stop the degradation of ubiquitin. One of these enzymes is USP7, a well-established oncology target, which plays a role in stabilizing oncogenic proteins and in the degradation of tumor suppressor p53.

Here, Weinstock et al. (DOI: 10.1021/ml200276j) describe a class of compounds that serve as dual inhibitors of the deubiquitylating enzymes USP7 and USP47, another target that plays a role in DNA damage response. The dual targeting could lead to a new class of compounds for the treatment of various cancers that synergistically inhibit the two independent pathways.

USE OF NMR IN IAPP AGGREGATION INHIBITION STUDIES



The aggregation of the islet amyloid polypeptide (IAPP) to form toxic assemblies is associated with the death of insulin-producing b cells in type 2 diabetes. One attractive therapeutic strategy is to inhibit the aggregation of IAPP. Natural polyphenols such as curcumin, present in the Indian spice turmeric, are potential inhibitors. Currently, it is not known how these molecules affect the kinetics of IAPP aggregation, given that they interfere with kinetic studies conducted using thioflavin T fluorescence.

In this issue, Liu et al. (DOI: 10.1021/ml300147m) describe the use of NMR to overcome the complications of using fluorescence studies in studying the inhibition of IAPP. By plotting signal intensities versus time, the authors were able to determine the kinetic profile of amyloid formation by IAPP in the presence of curcumin. Results of the study could lead to the design of more effective inhibitors of IAPP aggregation.

Published: October 11, 2012

   dx.doi.org/10.1021/ml300281k | *ACS Med. Chem. Lett.* 2012, 3, 780–780