Synthesis of the Phytohormone [^{11}C]Methyl Jasmonate *via* Methylation on a C_{18} Sep Pak™ Cartridge

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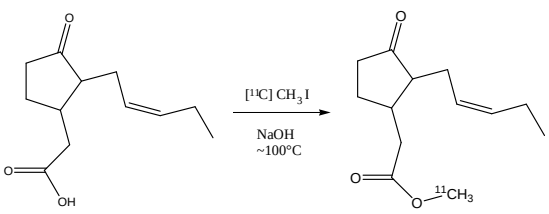
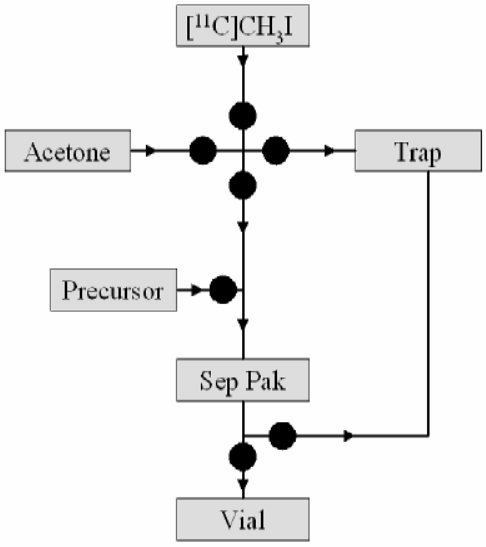
Introduction: Exposure of plants to jasmonates, a class of plant hormones, has been shown to increase growth rate,[1] production of defensive secondary chemicals [2] and lignins.[3] Recently, we have shown that jasmonates will increase leaf ^{11}C-sugar intermediates,[4] with subsequent increase in phloem loading and ^{11}C-sucrose partitioning to roots. Hence, we believe a role of jasmonates in resource partitioning and chemical fractionation may come from their regulation of sugar-transport proteins that mediate the long-distance transport of carbohydrates within the plant vasculature. The purpose of the present work was to develop a rapid method for introducing carbon-11 (t½ 20.4 min) into methyl jasmonate (MeJA). A key advantage for using this short-lived β^+-emitting radionuclide in plant biology is that tracer can be quantified *in vivo*, so that the same plant can be tested repeatedly over time. Additionally, the high specific activity achievable with ^{11}C allows us to administer non-physiological doses of tracer for observations of *in vivo* transporter binding. These measurements cannot be made with ^{14}C, ^{13}C or ^{3}H as tracers. The approach described in this work makes use of a solid-supported ^{11}C-methylation reaction.[5] This approach holds significant appeal for ease of experimental setup, and minimal effort to purify the final product.

Results and Discussion: [^{11}C]Labeled (±)-methyl jasmonate was synthesized using a C_{18} Sep Pak™ at ~100°C to sustain a solid-supported ^{11}C-methylation reaction of sodium (±)-jasmonate using [^{11}C]methyl iodide. After reaction, the Sep Pak was rinsed with acetone to elute the labeled product, and the solvent evaporated rendering [^{11}C]-(±)-methyl jasmonate at 96% radiochemical purity. The substrate, (±)-jasmonic acid, was retained on the Sep Pak so further chromatography was unnecessary. Total synthesis time was 25 min from the end of bombardment (EOB) which included 15 min to generate [^{11}C]methyl iodide using the GE Medical Systems PET Trace MeI system, 5 min for reaction and extraction from the cartridge, and 5 min to reformulate the product for plant administration. An overall radiochemical yield (at EOB) of 17 ± 4.3 % was obtained by this process, typically producing 10 mCi of purified radiotracer. A specific activity of 0.5 Ci/µmol was achieved using a short 3 min cyclotron beam to produce the starting ^{11}C.



Conclusions: (±)-[^{11}C]Methyl jasmonate was successfully produced in a short time, with high radiochemical purity of 96%, and in sufficient quantities that will allow for topical administration of tracer to intact leaves of plants. Although tracer specific activity was low, using larger starting amounts of ^{11}C might be expected to improve on this. The method described—using a disposable C_{18} Sep Pak—has great appeal due to the ease of setup. The approach is amenable to automation, or at least remote operation, in order to minimize personnel exposure to radiation hazards. This is essential if we are to use tracer for receptor imaging.



Schematic diagram of the reaction system

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Acknowledgement:
This work was part of an ISAP exchange between the University of Mainz and the State University of New York at Stony Brook, 2004. Support by the DAAD is gratefully acknowledged.