# Microfluidic [$^{11}$C]-carbonylation reactions for the rapid synthesis of radiolabelled compounds for PET

P-076

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Introduction: The synthesis of 11C compounds for PET requires fast and specialised chemical techniques owing to the short half-life of the 11C radioisotope (t1/2 = 20.4 min) and sub-micromolar reaction scales. [1] Microfluidic reactors are emerging as a valuable technology for the rapid and small scale synthesis of short-lived radiopharmaceuticals for PET imaging. [2] The palladium mediated 11C-carbonylation reaction is a highly versatile route for the preparation of a wide range of 11C-carbonyl compounds[3], however, the low molecular concentrations of 11CO coupled with its poor solubility in organic solvents make this a particularly challenging transformation. Here we report the application of a microfluidic reactor for improving the synthesis of 11C labelled amide and ester molecules via the palladium mediated 11C-carbonylation reaction.

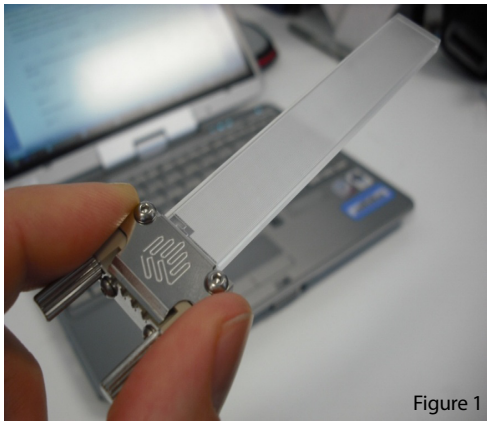
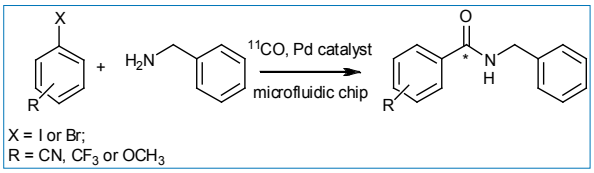


Figure 1

Methods: The microfluidic reactor (figure 1) was fabricated from glass using chemical wet etching techniques and contains two inlets, one outlet and a 5 metre long reaction channel. A simple mixing tee motif is used bring the gas and liquid reagents into contact with each other. The palladium mediated 11C-carbonylation reaction of a range of aryl halides was investigated (scheme 1). In a typical 11CO labelling experiment the coupling reagents (aryl halide, palladium catalyst and amine) were premixed and loaded into a 50 uL loop on an injector port. 11CO, produced via the high temperature reduction of 11CO2 over Mo, was preconcentrated and trapped onto molecular sieves. The coupling reagents were injected into the microfluidic device while at the same time 11CO was released from the molecular sieves and passed into the device for reaction.

Results: The total reaction and processing times for a typical reaction, including trapping and release of 11CO, was 15 min from end of bombardment. A series of amide and ester molecules were labelled with 11C using our microfluidic reaction system (scheme 1). Radiochemical yields (RCY) of labelled products were found to be dependent on the type of aryl halide and nucleophile used for the reaction. Generally, iodoaryl substrates with activating groups (CF3 or CN) gave consistently higher RCYs (>80%) and radiochemical purities (>95%) than aryl halide substrates with deactivating groups (OCH3).




Scheme 1

Conclusions: A glass fabricated microfluidic device has been used to effectively perform high speed 11CO radiolabelling reactions. The larger surface area-to-volume ratio within the microfluidic reactor improves the gas liquid contact area and is thought to enhance the problematic CO insertion step of this reaction.

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**References:**

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