Evolution of a High Yield Gas Phase $^{11}CH_3I$ Rig at LBNL

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After working with a home built "wet method" [^{11}C]methyl iodide system for a number of years, an effort was made towards the in-house development of a gas phase rig. This began with personal communication and visits to both TRIUMF and the University of Washington, Seattle PET centers for many helpful discussions, photos, drawings and hints that only years of experience can provide. The culmination of this was the construction of a first iteration single pass, gas phase [^{11}C]methyl iodide system that closely resembled the Seattle system described by Link[1].

The Biomedical Isotope Facility (BIF) at the Lawrence Berkeley National Laboratory houses the prototype CTI RDS111 (E_{proton} = 11MeV) negative ion cyclotron. We run an original 7mL aluminum-body target filled to 300psi with 1% O_2/N_2 to produce [^{11}C]CO_2. Typical production irradiations are 40 minutes in duration at 35uA beam current and provide on average 1.5Ci of [^{11}C]CO_2 that is most often converted to [^{11}C]CH_3I. Operation of the [^{11}C]CH_3I system is as follows: (a) Post irradiation, target gas is rapidly unloaded through a Carbosphere trap (60-80 mesh, 1.4g) at room temperature. Discussions with Bruce Mock led us to choose this trapping medium over molecular sieves for the chromatographic properties providing trapping of the [^{11}C]CO_2 and separation from target gas and side products. (b) After static heating of the trap to >80°C, the trap is swept with helium (50mL/min) and combined with hydrogen (50mL/min). (c) The mixture is passed through a heated (400°C) nickel catalyst (Harshaw) and the resulting [^{11}C]CH_4 is trapped on a PoroPak-Q trap (100mg in aluminum u-tube, 2mm id x 90mm tall) at -196°C. (d) The [^{11}C]CH_4 is released by raising the trap from the liq-N_2 dewar and flushing with helium (80mL/min) directing the gas stream through a quartz reaction tube (10mm id x 350mm). The head of the tube is packed with solid iodine that is heated to provide I_2 vapor which mixes with incoming [^{11}C]CH_4 and is pushed further downstream into a high temperature segment (100mm long) where conversion takes place. (e) The resulting [^{11}C]CH_3I exits the quartz reactor, is passed through a dry ascarite column (7mm id x 150mm), and is trapped on a glass test tube (4mm id x 50mm) immersed in liq-N_2.

Single-Pass Optimization

Significant optimization of the single pass system was initially required to generate useable yields and purity of [^{11}C]CH_3I. There are primarily three parameters that govern the overall conversion of [^{11}C]CH_4 to [^{11}C]CH_3I in the system, namely: (1) Iodine oven temperature (I_2 concentration); (2) flow through the reactor tube (residence time); and (3) temperature of the reactor (energy potential). These three factors are highly interdependent, thus changing any one parameter requires a re-optimization of the other two. For example, higher quartz tube (reactor) temperatures may require a faster flow rate and lower iodine oven temperature to decrease the co-production of [^{11}C]CH_2I_2 and maintain [^{11}C]CH_3I yield. Through this process we experimentally determined a push gas flow of 80mL/min and I_2 oven temperature of 70°C and then re-explored a range of reactor temperatures. Over a range of 625-775°C, the undesired production

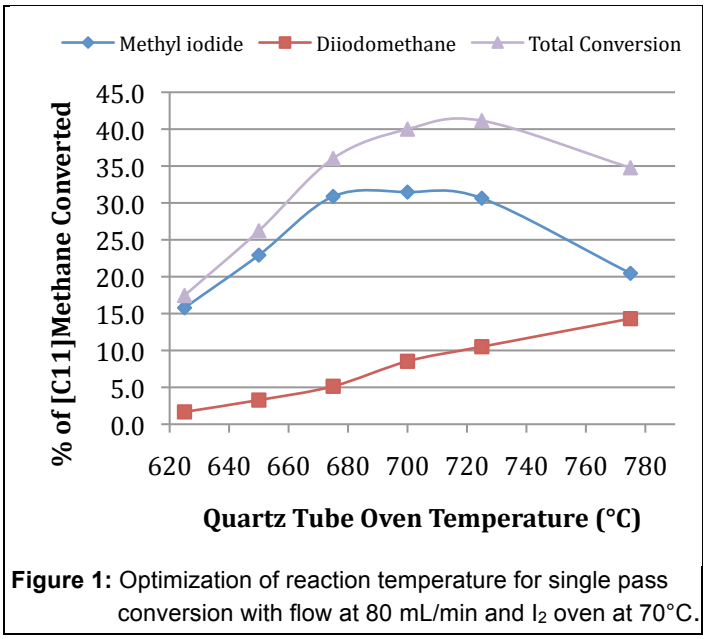

Figure 1: Optimization of reaction temperature for single pass conversion with flow at 80 mL/min and I_2 oven at 70°C.

of [^{11}C]CH_2I_2 increased linearly from 1.5-15%. Over the same temperature range (625-775°C), [^{11}C]CH_3I yield started at 15.5%, peaked at 32% (680°C) and fell back to 21%. Total conversion of methane to iodinated species followed a similar curve as shown in **Figure 1**. Consistent yields of 25-30% were realized for production runs for a number of months.

Recirculation System In order to increase the conversion yield we installed a recirculation pump in the system, passing the unconverted [^{11}C]CH_4 back to the reactor as described by Larsen[2]. In addition, we have separated the conversion oven from the [^{11}C]CH_4 and [^{11}C]CH_3I trapping station allowing vertical placement on the hotcell side wall thus saving space. At the exit of the oven, a vortex chiller (-8°C) rapidly condenses I_2 vapor ensuring nearly complete iodine recovery. Other refinements to the system include a low mass Kapton resistive heater on the I_2 reservoir and a LED/photodiode based I_2 concentration detector.

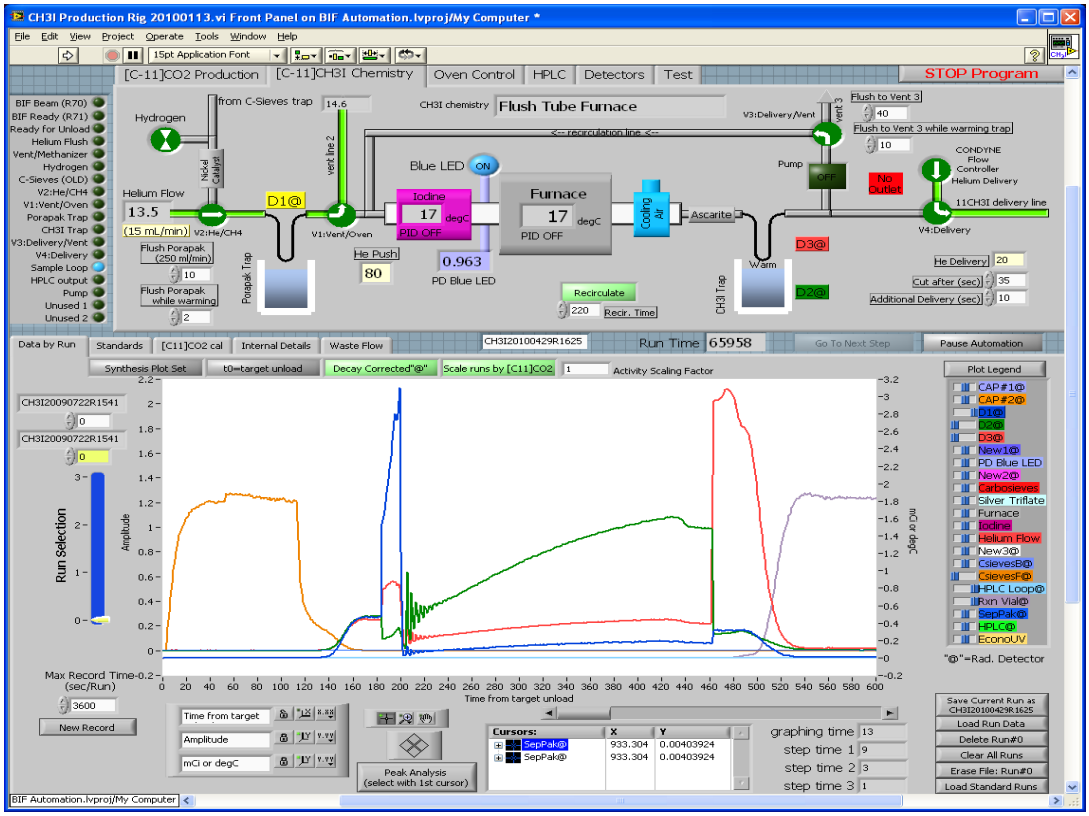

Figure 2: Screenshot of LabVIEW based software control panel on BIF methyl iodide rig.

With very little modification to either equipment or parameters we were able to realize a significant gain in conversion yield as compared to the single-pass setup. Optimized conditions provide 64-73% decay corrected yield of [^{11}C]CH_3I based on trapped [^{11}C]CO_2 with >98% purity. The high purity is attributed to cryogenically trapping the iodinated methane in a glass loop, releasing the [^{11}C]CH_3I while the glass warms, and recooling the glass before the [^{11}C]CH_2I_2 is pushed to the reaction vial.

Over the past 5 years we have seen 50-60% conversions on a daily basis. Maintenance is minimized by having the [^{11}C]CH_4 Poropak trap outside of the recirculation path, trapping iodine at -8°C, and cold trapping the [^{11}C]CH_3I on a glass trap. We have routinely used this system to produce a variety of [^{11}C] labeled PET tracers at or above literature yields and high specific activity (5-12Ci/umol eos).

References:

[1] Link, J., Krohn, K., Clark, J., 1997. Production of [^{11}C]CH_3I by Single Pass Reaction of [^{11}C]CH_4 with I_2. Nucl. Med. Biol. 24, 93-97

[2] Larsen, P., Ulin, J., Dahlstrom, K., Jensen, M., 1997. Synthesis of C-11 iodomethane by iodination of C-11 methane. Appl. Radiat. Isot. 48, 153-157