

Ion Exchange Trap and Release of [¹¹C]CO₂

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Introduction

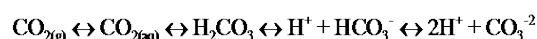
Recently in our laboratory we needed a reliable and relatively simple source of aqueous solutions of [¹¹C]CO₂. We examined various methods of trapping [¹¹C]CO₂ gas both in solution and on ion exchange resins, followed by elution into aqueous phase. We favor simple methods that have high trapping and elution efficiencies and produce a highly concentrated solution. Furthermore, we desired methods that would minimize the use of hazardous reagents and materials with respect to both handling and disposal. We also considered the formulation of the final solution in terms of chemical compatibility with contacted materials, working with the assumption that dilute bicarbonate or carbonate solutions will have little reactivity with many materials. In a phantom, compatibility with materials (i.e. plastics, glues, metals, etc.) is important (1-4), while in (bio)geochemical studies – where transport of carbon is important – the chemical form of the radiolabelled molecule is important, but compatibility must be determined on a case-by-case basis (5-7).

Small medical cyclotrons can easily produce carbon-11 as gaseous [¹¹C]CO₂, and various methods are utilized to incorporate carbon-11 into solution, often with unfavorable resource requirements, costs, or chemical properties. Commonly [¹¹C]CO₂ gas is bubbled through a strong base, forming the carbonate anion; but neutralizing a strong base (as to avoid special handling or disposal requirements) requires a large volume of diluent or buffer; or a very precise addition of acid – which if done improperly – may lead to an acidic pH and subsequent loss of [¹¹C]CO₂ from solution (8,9). Alternatively, [¹¹C]CO₂ (or [¹¹C]CH₄) can be converted to [¹¹C]CH₃I at high-yield, but requires specialized, expensive radio-synthesis equipment (10-12). [¹¹C]CH₃I can then be trapped in DMSO (albeit providing a volatile and hazardous solution) or used as a synthon en route to water soluble compounds such as [¹¹C]choline (13). Finally, leftover radiolabelled radiopharmaceuticals from a carbon-11 imaging experiment could be used, but chemical compatibility (i.e. lipophilicity) of the radiolabelled compound may be of concern.

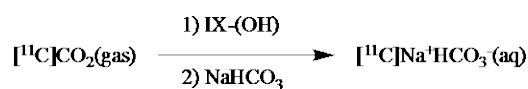
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[#]This work is an ongoing continuation of published results (ref 16).

Carbon dioxide gas will dissolve with a solubility of 1.5 g/L at STP (9) and slowly react with water to generate carbonic acid (H₂CO₃), a weak acid.



Passing [¹¹C]CO₂ through a base-activated ion exchange cartridge, the [¹¹C]CO₂ reacts with hydroxide ions to form [¹¹C]carbonate which is bound to the resin due to its higher selectivity for carbonate than hydroxide (14). Elution with excess bicarbonate displaces [¹¹C]carbonate and neutralizes any remaining hydroxide, providing a ¹¹C aqueous solution that is mildly basic, chemically non-hazardous, and very concentrated.



Material and Methods

[¹¹C]CO₂ gas trapping efficiency was evaluated for solutions and base-activated ion exchange resins. The gas was delivered either rapidly in a high-flow bolus directly from the cyclotron target or slowly in a low-flow helium stream during heating of a carboxiesieves column. Elution efficiency of ion exchange cartridges were evaluated for both fraction of trapped activity eluted and volume of solution needed for elution.

[¹¹C]CO₂ was produced via the ¹⁴N(p,α)¹¹C reaction on a CTI RDS111 – 11 MeV cyclotron at the Lawrence Berkeley National Laboratory's Bio-medical Isotope Facility. The 7 mL target is pressurized to 315 psi with 1% O₂/N₂ gas, equating to 150 mL gas at STP. For direct-from-target trapping experiments, the target was decompressed and routed to the cartridge via 50 feet of 0.020" I.D. tubing until the target falls to atmospheric pressure (~55 seconds) providing an inhomogeneous flow – a short rapid burst of flow followed by a longer low-flow bleed. For helium-eluted experiments, the [¹¹C]CO₂ was unloaded from the cyclotron target and trapped

on a room-temperature carbo sieves column (15). Target gases were subsequently flushed from the column for 30 seconds with helium at 50 mL/min. After heating the column to 125 °C without gas flow, [¹¹C]CO₂ was eluted off the column in helium at 15 mL/min.

[¹¹C]CO₂/He was bubbled through 9 aqueous and 2 organic solutions to test for trapping efficiency in a slow, steady helium stream at 15 mL/min (sodium hydroxide (0.96M, 0.096M, 0.0096M), sodium bicarbonate (1.14M, 0.57M, 0.057M), sodium carbonate (2.0M, 1.0M, 0.10M), ethanol, and DMSO (2mL ea.)). An Ascarite-filled cartridge was attached to trap any untrapped [¹¹C]CO₂. Measures of radioactivity were made using a Capintec CRC-15R dose calibrator. Trapping efficiency for solutions is calculated as the fraction of radioactivity captured in solution relative to the sum of the solution and the Ascarite trap.

Three different commercially available, ion exchange cartridges were evaluated for trapping and elution efficiencies. FIGURE 1 shows a photographic comparison of the physical size and shapes of the cartridges as well as a X-ray computed tomography (CT) cross sectional view of the internal ion exchange resin volume and dead volume of the cartridges.



FIGURE 1. Photo and X-Ray of IX Cartridges (L-R, Alltech IC-OH, ORTG, Waters QMA)

All cartridges were activated with 1 mL of 1 N aqueous NaOH followed by passing 10 mL deionized water then 10 mL of air through the cartridge.

In both direct-from-target ($n = 4$) and helium-stream experiments ($n = 3$ or 4), cartridges were connected to [¹¹C]CO₂ delivery lines via Luer connections. The gas exiting the cartridge passed through an empty 3 mL crimp-top vial as a liquid trap en route to an Ascarite trap on the vent needle as described above. Trapping efficiency for cartridges is calculated as the fraction of radioactivity captured on the cartridge relative to the sum of the cartridge, the empty vial, and the Ascarite trap.

Cartridges were eluted with 0.5 mL of saturated sodium bicarbonate solution (1.14 M @ 20°C) followed by 9.5 mL water and 10 mL air. Elution efficiency is calculated as the fraction of radioactivity eluted in 10 mL relative to the sum of the spent cartridge following elution and the 10 mL eluate (Equation 5). The pH of the eluate was measured using 0-14 pH test strips.

Results and Conclusion

The trapping of [¹¹C]CO₂ in all solutions was less than 70% of the total radioactivity with the exception of the 0.96 M and 0.096 M NaOH. With a higher concentration of base driving equilibrium towards carbonate stability, it could be expected that the most basic solution had the best trapping efficiency, but this attribute also means it is least desirable solution to work with from a hazardous material or chemical compatibility perspective.

When [¹¹C]CO₂ was delivered in a helium stream, all three cartridges performed at near 100% efficiency, as shown in FIGURE 4. With higher flow, direct-from-target delivery, the cartridges trapped [¹¹C]CO₂ with a wider range of efficiencies: ICOH ($99 \pm 1\%$), ORTG ($90 \pm 2\%$), and QMA ($79 \pm 4\%$). Elution resulted in $> 99\%$ release of carbon-11 activity for both QMA and ORTG cartridges, but only $39 \pm 3\%$ release from the ICOH cartridge. Elution efficiency of the trapped radioactivity (Equation 5) was independent of the method of [¹¹C]CO₂ delivery. Across all cartridges and delivery methods, the eluate was at about pH = 10.

We recommend that the ORTG cartridge be used for trapping of [¹¹C]CO₂ gas with elution by > 300 μ L of saturated bicarbonate solution. This recommendation is based on the better trapping for ORTG cartridges compared to the QMA cartridges in the direct-from-target [¹¹C]CO₂ delivery method and the smaller volume needed for elution of all trapped carbon. This method excels based on its simplicity, adaptability to automation, low-cost (\$5/cartridge), and observations that a single ORTG cartridge suffers no loss of performance after multiple uses. A potential disadvantage to this method is that it involves using a carbon-containing eluent, which means that this method cannot be used for imaging experiments that require high specific activity. However, considering the eluate is a mildly basic aqueous solution, we expect that it will be compatible with a wide variety of materials and experimental applications.

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Acknowledgements

The authors would like to thank Dr. Mustafa Janabi, April Van Hise, and Steve Hanrahan for their contributions.

This work was supported by the Director, Office of Science, Office of Biological and Environmental Research, Biological Systems Science Division of the U.S. Department of Energy under Contract No. DE-AC02-05CH11231.