

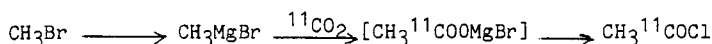
SYNTHESIS OF NCA [carbonyl- ^{11}C]ACETAZOLAMIDE FOR PET STUDIES IN VIVO

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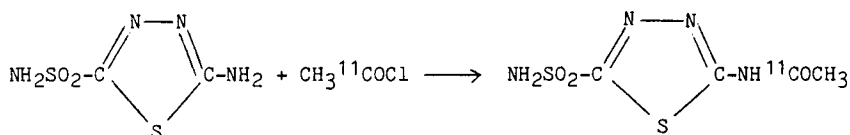
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Acetazolamide, Diamox or 5-acetamido-1,3,4-thiadiazole-2-sulphonamide, is a well known and widely used inhibitor of carbonic anhydrases (EC 4.2.1.1.) (1). These enzymes catalyse the interconversion of carbon dioxide and water with carbonic acid and are found in a variety of tissues. In order to provide some possibility for studying the distribution of carbonic anhydrases *in vivo* by PET, we have developed a method for labelling acetazolamide with the positron-emitting radionuclide, carbon-11 ($t_{1/2} = 20.3$ min).

The method is based on the acetylation of 5-amino-1,3,4-thiadiazole-2-sulphonamide with [$1\text{-}^{11}\text{C}$]acetyl chloride. For this purpose the amine is obtained by acid hydrolysis of acetazolamide itself (2), while [$1\text{-}^{11}\text{C}$]acetyl chloride is produced by the carbonation of methylmagnesium bromide with cyclotron-produced [^{11}C]carbon dioxide, followed by addition of phthaloyl dichloride plus 2,6-di-tert-butylpyridine (3):



Acetylation is achieved by brief (< 10 min) heating of the amine with [$1\text{-}^{11}\text{C}$]acetyl chloride in acetonitrile:



Separation and purification are achieved on a semi-preparative reverse-phase HPLC column, (30 cm x 0.7 cm i.d; μ -Bondapak C-18) eluted at 3 mL/min with potassium dihydrogen phosphate solution (0.07 M). Analytical HPLC and TLC show the collected radioactive fraction, (retention time 12 min) to be radiochemically (99%) and chemically pure (> 95%) [^{11}C]acetazolamide. This product is ready for intravenous injection after sterile filtration. The preparation requires 30 minutes and provides [^{11}C]acetazolamide in a radiochemical yield of 15% (decay-corrected to E.O.B.). Specific activity is in the range 300-350 mCi/ μmol corrected to EOB (giving 10 to 30 μg of carrier), when starting from an irradiation producing 250 mCi of [^{11}C]carbon dioxide.

[^{11}C]Acetazolamide is now under further investigation as a probe for carbonic anhydrases in the lung, heart and brain.

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