Synthesis and Separation of Chiral Compounds in the Preparation of a PET Radiotracer Targeting Synaptic Vesicle Glycoprotein 2A

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Positron emission tomography (PET) is a promising technology that utilizes radiotracers for producing detailed, 3D images of the body. The radiotracer studied in this project targets the SV2A receptor in the brain, which is a marker of synaptic density and hence can be used to study Alzheimer's disease and epilepsy. This project aims to synthesize an enantiopure compound in preparation of a chiral PET radiotracer. The racemic compound was synthesized at -20C and purified using a silica gel column. Reaction progress was monitored by thin layer chromatography and structure was confirmed utilizing NMR. Conditions required for separation using the HPLC system were optimized by testing varying combinations of organic solvents (0–100%), in conjunction with different chiral columns and flow rates (0.1 –2mL/min). Three chiral catalysts were tested under varying reaction conditions for synthesizing an enantiopure compound. The racemic compound was successfully synthesized and separated using the HPLC system. Full separation was achieved by using ethanol and hexane in a 25%/75% combination, 0.1% TEA, 1.0mL/min flow rate and the CHIRALCEL OJ-H column. The quinidine catalyst preliminarily yielded a successful 90/10 enantiomeric ratio on a tested compound. The other 2 catalysts produced a racemic compound. The quinidine catalyst is being tested under new conditions to further improve the enantiomeric ratio. Using chiral catalysts to optimize the synthesis of the radiotracer could increase product yield and lower the synthesis time and cost. This increases the viability of this PET radiotracer for diagnostics and research of Alzheimer's disease, epilepsy and other neurodegenerative diseases.

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