Synthesis of Ethyl-3-(Tert-Butylamino)-2-Phenylpropanoate: A Novel Dopamine Transporter Inhibitor

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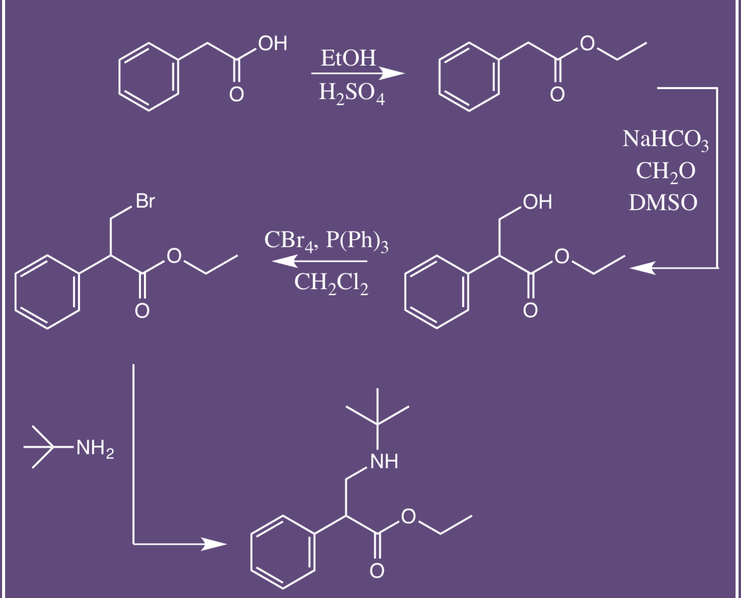
Introduction

Dopamine is a neurotransmitter that effects movement, cognitive function, and pleasure and pain interpretation, among other important functions. Dopamine levels have a direct connection to addiction and diseases such as Parkinson's disease, schizophrenia and ADHD. After release into the synapse, dopamine is transported back into the presynaptic neuron by the dopamine transporter (DAT), controlling dopamine levels in the brain. Dopamine transport exhibitors block DATs and artificially raise dopamine levels. These inhibitors are useful compounds used to treat addiction, depression, and as cognitive enhancers. Bupropion is an antidepressant drug approved by the Food and Drug Administration (FDA) to treat seasonal affective disorder (SAD) and acts as a smoking cessation aid.[1] Because of its similarity to the structure of bupropion ,the molecule ethyl-3-(tert-butylamino)-2-phenylpropanoate was synthesized as a potential dopamine transporter inhibitor. By synthesizing new kinds of transporter inhibitors, the dopamine pathway can be better understood.

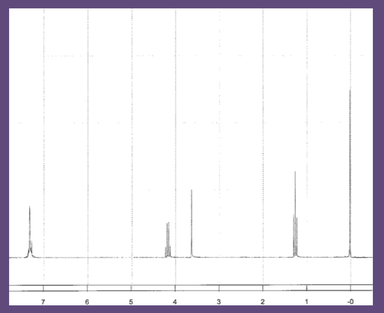
Synthesis[2,3,4,5]



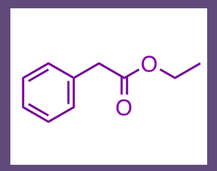
Conclusion

Phenylacetic acid was dissolved in ethanol with sulfuric acid to form ethyl-2-phenylacetate through esterfication. Product formation was confirmed using ^{1}HNMR spectroscopy. Upon reaction with sodium bicarbonate and paraformaldehyde in DMSO, ethyl-3-hydroxy-2-phenylpropanoate was formed. The product was separated from the starting material by column chromatography. This product formation was confirmed using ^{1}HNMR spectroscopy. The alcohol can then be converted to a halogen, and when reacted with a nucleophile such as 2-methylpropan-2-amine form the final product. The last two steps were unable to be completed as a result of the small yield of the second step. Once the second step is optimized, the synthesis can be completed. The chloro-substituted forms of both of these products were also able to be formed and confirmed using ^{1}HNMR spectroscopy.

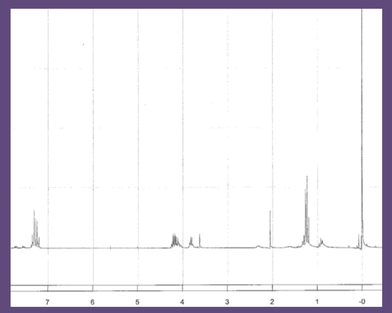
^{1}HNMR Spectra



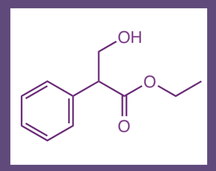
Ethyl-2-phenylacetate spectra



Ethyl-2-phenylacetate structure



Ethyl-3-hydroxy-2-phenylpropanoate spectra



Ethyl-3-hydroxy-2-phenylpropanoate structure

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