Synthesis of 2-Benzhydrylpiperidine, a Novel Dopamine Transporter Inhibitor

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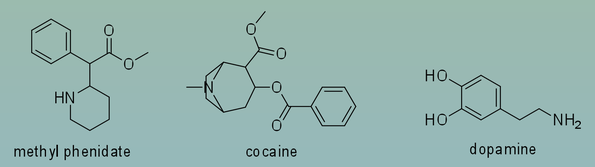
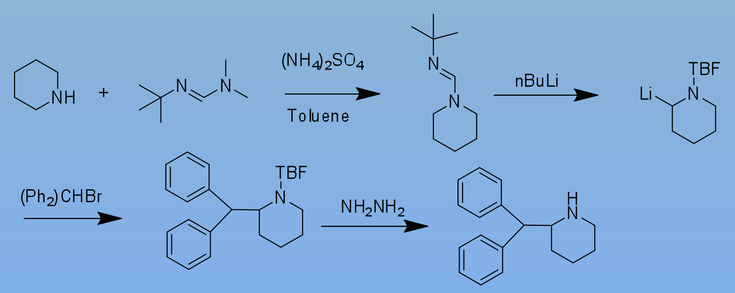
Introduction

Dopamine is a crucial neurotransmitter that plays a significant role in brain processes such as cognition, memory, learning, and sleep patterns.[1] Dopamine is stored and synthesized in the neurons of the substantia nigra which is located in the midbrain. Diseases that affect the dopamine pathway include attention-deficit hyperactivity disorder (ADHD), depression, narcolepsy, shift work sleep disorders, Parkinson's disease, schizophrenia, and drug addiction.[3] The dopamine transporter (DAT) is a protein that regulates the amount of dopamine in the synapse. Dopamine transporter inhibitors are a class of drugs that have been gaining importance for the ability to treat the many diseases which interfere with the dopamine pathways. Dopamine transport inhibitors act as a reuptake inhibitor of dopamine and block the DAT.[2] This causes an increase in the extracellular concentrations of dopamine, which leads to feelings of increased pleasure and enhanced cognition.[1] The ultimate goal is to propose a synthesis for 2-benzhydrylpiperidine which has the potential to be a dopamine transport inhibitor and contains the partial structures of modafinil and methyl phenidate.

Compounds of Interest



Experimental Synthesis



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Conclusion

In the four proposed steps of the synthesis the first step was carried out and only the crude product was obtained. The purification method of column chromatography was not successful because ^{1}HNMR analysis confirmed that the product was never isolated from the column. Future work on this synthesis will need to take into consideration the optimization of the purification of the first synthetic step. This can be done by changing the polarity of the solvent of 93:7 hexanes: triethylamine to 80:20 hexanes: triethylamine.

Another useful method for the purification process is using distillation techniques. Distillation techniques are useful because they separate the mixtures based on the volatilities and not the polarities.

References

1. Dopamine: A Sample Neurotransmitter. http://www.utexas.edu/research/asrec/dopamine.html (Accessed November 15, 2011).
2. Dopamine Transporter. http://www.rndsystems.com/molecule_detail.aspx?m=3391 (Accessed November 13, 2011).
3. J. M. Fellous, R. Suri. The Handbook of Brain Theory and Neural Networks, 2nd ed; Cambridge, Ma: The MIT Press, 2002.