



CALIFORNIA STATE SCIENCE FAIR  
2008 PROJECT SUMMARY

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<b>Project Title</b> Synthesis of a Substituted Carbamate for Imaging Acetylcholinesterase	
<p style="text-align: center;"><b>Abstract</b></p> <p><b>Objectives/Goals</b> The goal was to synthesize a carbamate, bromomethylphysostigmine (BMPHY) for use as an imaging agent for Alzheimer's Disease using positron emission tomography (PET). This required reaction of a substituted phenol or phenolate with bromoethylisocyanate (BEI). BEI has two reactive positions, the isocyanate group or the bromide atom. The goal of this project was to establish reaction conditions: 1. Conduct pilot reaction of phenol with BEI to evaluate formation of N-bromoethylphenylcarbamate (BEPC); 2. React eseroline and BEI for the formation of the desired product, BMPHY.</p> <p><b>Methods/Materials</b> Sodium hydride (NaH), potassium tert-butoxide (KOBu), tetrahydrofuran (THF), diethyl ether (DEE), eseroline, BEI, dichloromethane, NaHCO<sub>3</sub> were from Sigma-Aldrich. TLC and electrospray mass spectra analyses were obtained on samples. Phenol (94 mg) was dissolved in 1 mL DEE and in THF (1 mL). 2 vials of DEE and 2 of THF were without base; 2 (one DEE and one THF) with KOBu, 112 mg and 2 (one DEE and one THF) with NaH, 42mg. BEI (0.09 g) was added and reaction monitored. Without base reactions were checked at 25 oC and 50 oC. To eseroline (15 mg) in DEE (1 mL), KOBu (5 mg) or NaH (4 mg) was added. After 15 mins, BEI (0.004 mL) was added. After 30 mins water (0.5 mL) was added. The ether layer was separated and checked by TLC and mass spectrometry. A similar set of reactions were carried out in THF.</p> <p><b>Results</b> For phenol no reaction occurred in the absence of base. With base, THF dissolves the phenolate salts better compared to DEE. The best yields of product were obtained with THF and KOBu. The next best was DEE and NaH. The product, BEPC was confirmed by TLC and mass spectra (M+H = 244, 246 and M+Na = 266, 268). This can partially be explained by solubility, but the reaction may be more complex because of the bromine atom present leading to complex side products. In the case of eseroline, the best solvent was found to be DEE rather than THF because the reaction was cleaner with little side products. BMPHY was confirmed by TLC and mass spectra ( M+H = 368, 370 and M+Na = 390, 392).</p> <p><b>Conclusions/Discussion</b> The two new products, BEPC and BMPHY were successfully synthesized. THF and KOBu gave the highest product yield in the case of the model phenol reaction, but not for the reaction of eseroline and BEI. The yields were significantly lower. Best yields were obtained when DEE was used with eseroline.</p>	
<b>Summary Statement</b> A substituted carbamate was successfully synthesized for potential use in imaging Alzheimer's Disease.	
<b>Help Received</b> Used Laboratory equipment at University of California - Irvine under supervision of Dr Jogesh Mukherjee	