CHARGE NUMBER: 2500

PROJECT TITLE: Synthesis of Tobacco Additives

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PROJECT LEADER: J. I. Seeman

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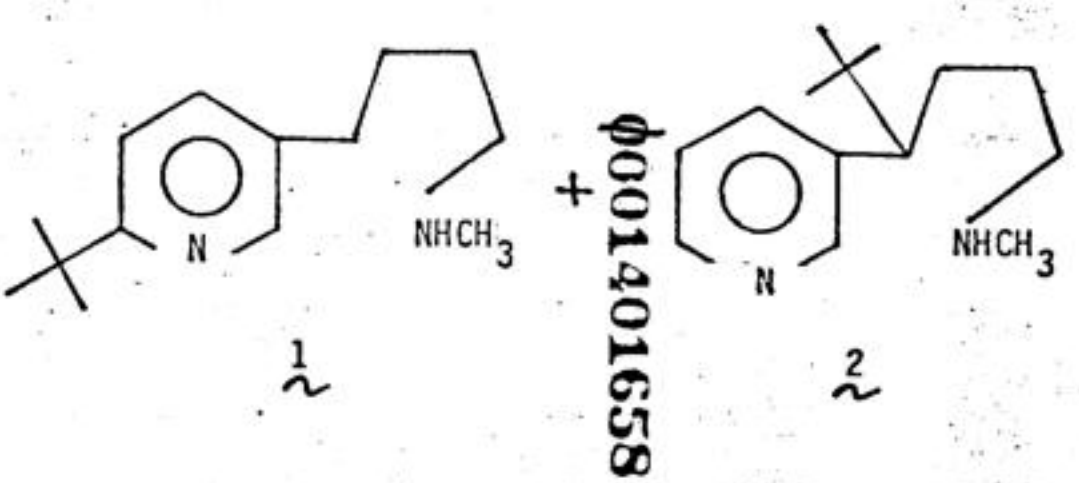
I. NICOTINE CHEMISTRY

The first separation of nicotine analogue isomers has been successfully completed using HPLC methodology. This achievement is of major importance in that it will allow us to purify 2-methylnicotine, 4-methylnicotine, and 6-methylnicotine produced from the methylation of nicotine. The first and key stage in this HPLC development was the separation of the above isomers by thin layer chromatography; very careful and tedious efforts led to an appropriate solvent system[1] which was subsequently adapted to HPLC use by fine-tuning the solvent mixture.[2] We are currently examining this method for other difficult separations.[1]

We have solved the riddle of non-reproducibility of aberrant products 1 and 2 in the reaction of t-butyllithium with nicotine (see eq. 1). Two highly unusual products result when the reaction is run at 0° in THF and reproducibility is observed when the system is completely deoxygenated. The source of the two aberrant products was evaluated by examining the reaction of dihydrometanicotine and methyl dihydrometanicotine with t-butyllithium. To check the generality of the aberrant product, we carefully examined the reaction of isopropyllithium with nicotine; at -70° and at 0°, no significant aberrant isopropyl product was obtained and 6-isopropylnicotine was the major product.[3,4]

(1) Nicotine + t-Butyllithium ⟶  +

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