SILICA AS A MEDIUM FOR THE SYNTHESIS OF CHIRAL IMINES AND CHIRAL AMINES

Mehvish Durrani, Marlie Kolb, Cortney Taylor, Dr. John Barbas
Department of Chemistry, College of Science and Mathematics, Valdosta State University

ABSTRACT

During the last few years we have been investigating greener and more economical methods for a one-pot synthesis of chiral imines and amines. We have synthesized several of these compounds quantitatively, in reactions between chiral amines and aromatic aldehydes, substituted with electron withdrawing groups, and electron donating groups, at the ortho, meta, and para positions. All reactions take place in minutes at room temperature. Typically, 2 grams of activated silica are suspended in the minimum amount of dry ether or other solvent. To this suspension, equimolar quantities of an aldehyde and a chiral amine are added successively, while stirring. Formation of the chiral imine is complete in a few minutes, as confirmed by GC-MS. At this point, the imine can be isolated or converted to the amine, as desired. For the reduction step, the suspension is cooled in an ice bath, followed by the addition of pulverized sodium borohydride. To this mixture, a few drops of water are added periodically and stirred briefly. Completion of the reduction to the amine is monitored by GC-MS. The products are extracted from silica with dry ether, dried over anhydrous sodium sulfate, and the solvent is removed under vacuum. The products are weighed and analyzed by IR, GC-MS, and ^{1}H/C-13 NMR. The samples are further purified by column chromatography to remove trace impurities before obtaining specific rotations.

BACKGROUND

Currently, the most common synthesis of amines is carried out by using large amounts of carcinogenic benzene as a solvent. Benzene is refluxed and distilled multiple times in order to synthesize the product and remove the solvent. In order to purify the amine, the mixture has to be heated and distilled. However, heat decomposes the final product and thus the percent yield is at best about 70%. The synthesis itself takes several days, consumes large amounts of energy and is environmentally unfriendly.

MATERIALS AND METHODS

Two grams of dry, activated silica were introduced into a dry round bottomed flask equipped with a stirring bar and a drying tube. 1.0x10^{-3} mol of an aldehyde and 1.0x10^{-3} mol of the chiral amine were transferred to this flask using about 20 mL of dry ether. The aldehyde can vary, but the amine stays the same, only varying in (R) or (S) configuration. The mixture was stirred for about 30 minutes to produce quantitatively the imine intermediate. The imine product was checked using GC/MS. When the solution was pure imine, the specific rotation was taken. To produce the amine from the imine, about 0.15 grams of sodium borohydride were introduced to the flask and stirred briefly. The flask was cooled in an ice bath and reduction was initiated by periodically adding a few drops of water. Subsequent washing and filtration of the silica occurred with several aliquots of ether. The extracts were combined, and the ether was removed using a vacuum and rotavapor combination. The remaining product, chiral amine, was analyzed using GC-MS, proton NMR, C-13 NMR, and if applicable, F-19 NMR.

SYNTHESIS OF 4-(TRIFLUOROMETHYL) BENZYL-α-METHYLBENZYLAMINE

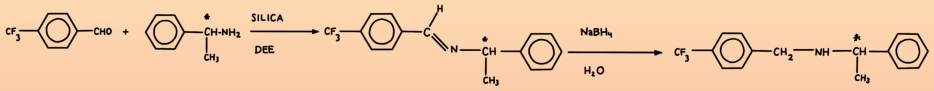


Figure 1: Reaction Mechanism

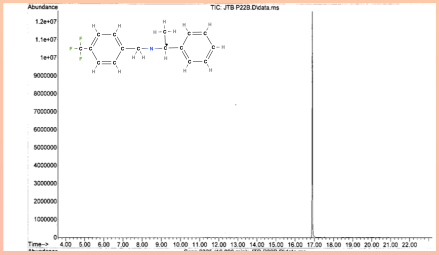


Figure 2: GC/MS of final amine confirms the product.

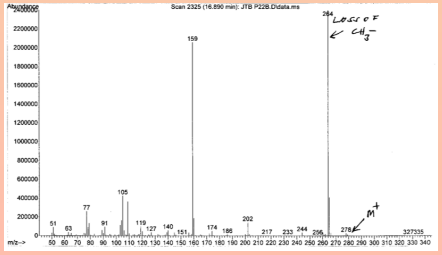


Figure 3: GC/MS of final amine confirms the product.

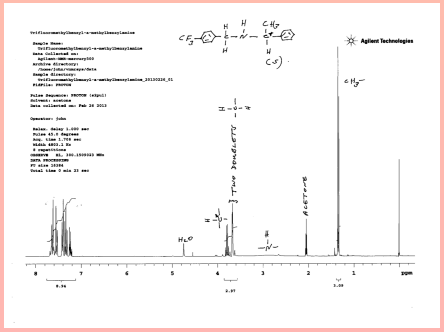


Figure 4: Proton NMR of amine.

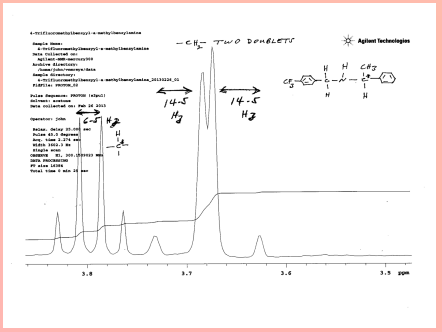


Figure 5: Expanded region of two doublets in proton NMR.

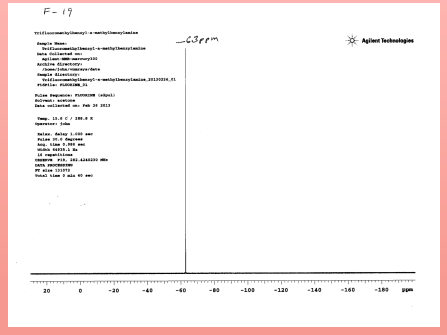


Figure 6: F-19 NMR of amine.

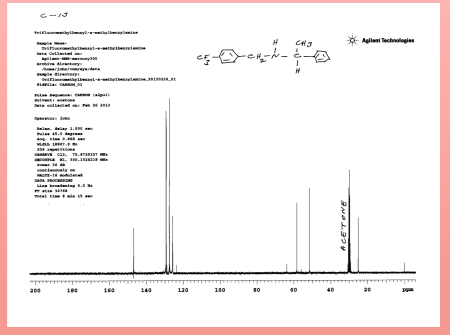
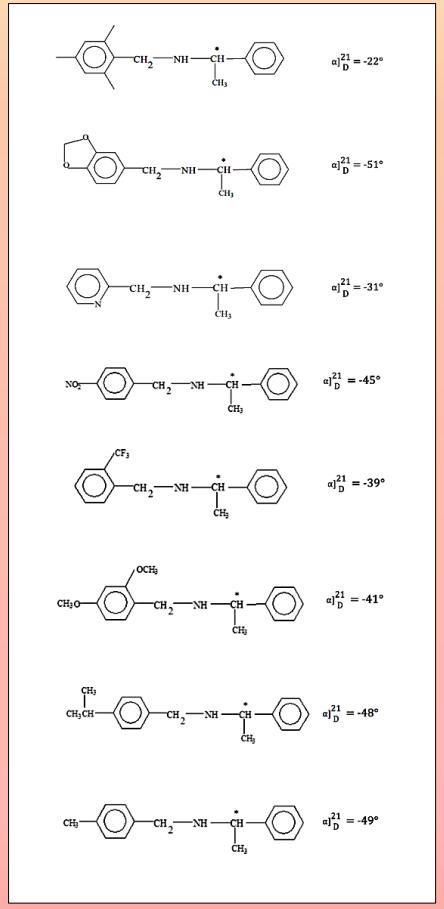


Figure 7: C-13 NMR of amine.

SPECIFIC ROTATION OF SEVERAL (S)-AMINES SYNTHESIZED ON SILICA



CONCLUSION

This method of synthesis lasts several hours at the most, uses very small amount of solvent and thus is energy efficient. Not only is this a greener method than the current procedure used by the industry, but it also gives a 98% to 100% yields.