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Spotlight 158

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Ammonia: A Versatile Reagent in Organic Chemistry

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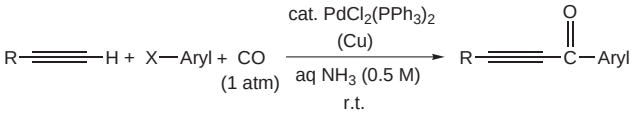
Introduction

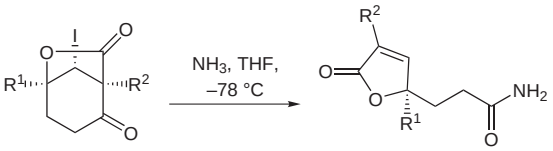
At standard temperature and pressure ammonia (NH_3) is a colourless gas with a characteristic pungent odor and is easily liquified. In addition to being used as a solvent in the form of liquid ammonia, it is very commonly employed as an aqueous solution or a gas. Ammonia has become a very important and versatile reagent used in organic chemistry. It is employed in a great variety of chemical reactions as Birch reductions,[1] Ugi reactions,[2] dechlorinations[1] and promotes a great series of important chemical transformations, such as Sonogashira coupling,[3] fragmentation of carbolactones[4] and many others. The examples below highlight the importance and great versatility of this reagent in organic synthesis.

Abstract

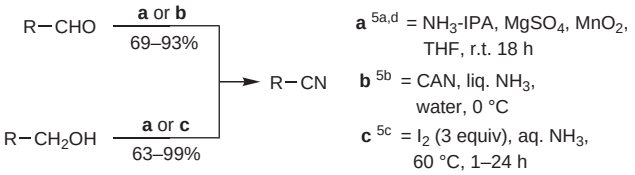
(A) Carbonylative Sonogashira coupling of terminal alkynes with aryl halides in the presence of 1 mol% of $PdCl_2(PPh_3)_2$, 2 equivalents of 0.5 M aqueous ammonia, and CO (1 atm) was found to proceed efficiently when dilute aqueous ammonia was used as an additive.[3]



(B) Ammonia promotes the fragmentation of 2-alkyl- and 2,4-dialkyl-3-iodo-1-oxocyclohexan-2,4-carbolactones providing butenolide compounds which are good precursors for the synthesis of piperidones and pyrrolidines.[4]



(C) Simple, effective, and high-yield procedures for direct oxidative conversion of primary alcohols and aldehydes to nitriles were successfully carried out in the presence of ammonia. Treatment of aldehydes with (a) manganese dioxide, magnesium sulfate and ammonia in propan-2-ol–THF at room temperature[5a] or (b) ceric ammonium nitrate (CAN) in ammonia–water[5b] provided the respective nitriles. Primary alcohols were also converted into respective nitriles by treatment with (c) molecular iodine in aqueous ammonia at 60 °C[5c] or even using the procedure given under (a).[5d]



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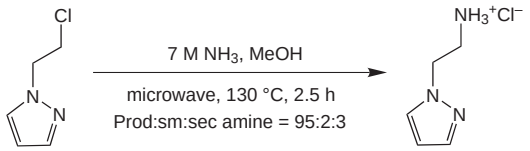
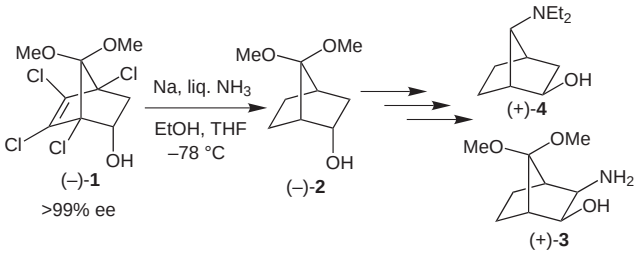
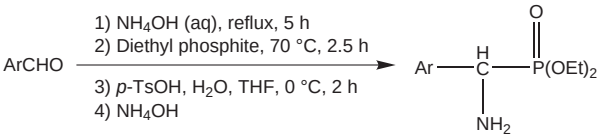
(D) A practical and atom-economical synthesis of hydrogen halide salts of primary amines, directly from the corresponding halides, using microwave irradiation in 7 M ammonia in methanol has been reported.[6] This procedure avoids the production of significant amounts of secondary amine side products, and requires only evaporation of the solvent to access the products in yields generally greater than 90%.



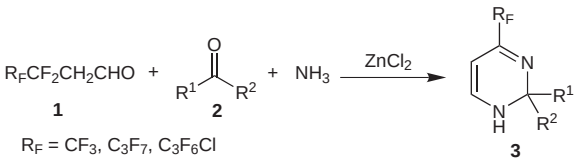
(E) The sodium/liquid ammonia system was utilized to dechlorinate and reduce the chiral compound (–)-**1** in high yield.[1] This compound is an important precursor for the synthesis of enantiopure amino alcohols **3** and **4**, which presented good results as chiral ligands in asymmetric reactions.[7a,b]



(F) A simple and efficient process for the synthesis of 1-aminophosphonic acids from simple starting materials was developed.[8] Treatment of aromatic aldehydes with ammonia and reaction with diethyl phosphite gives diethyl *N*-(arylmethylene)-1-aminoaryl methylphosphonates, which can be easily hydrolyzed to diethyl 1-aminoarylmethylphosphonates. This method is easy, rapid and gives 1-aminoalkylphosphonates in good yields.



(G) Liu and co-workers[9] described an unexpected tri-component reaction between **1**, aldehydes, ketones or enol ethers and ammonia in the presence of zinc chloride, providing a facile synthetic method for 4-fluoroalkyl-1,2-dihydropirimidines **3**, instead of the Mannich-type products. These compounds are useful intermediates for the synthesis of various fluorine-containing compounds of biological interest.



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