

SYNLETT Spotlight 144

Silver Nitrate: Versatile Reagent in Organic Synthesis

Compiled by Amit Nayyar



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

Amit Nayyar was born in Nadaun, Himachal Pradesh, India in 1978. He studied for his B.Pharm. from L. M. College of Pharmacy, Ahmedabad, India, then began his studies in medicinal chemistry in 1999 from National Institute of Pharmaceutical Education and Research, (NIPER), Mohali, Punjab, India, where he received M.S. (Pharm) degree. He worked as a research chemist at Discovery Research, Dr. Reddy's Laboratories Ltd, Hyderabad. Presently he is working for his Ph.D. under the tutelage of Dr. Rahul Jain. His research interests comprise of peptide synthesis and the synthesis of heterocycles having therapeutic importance.

Department of Medicinal Chemistry, National Institute of Pharmaceutical Education and Research (NIPER), SAS Nagar, Punjab 160 062, India

E-mail: mailnayyar@yahoo.com

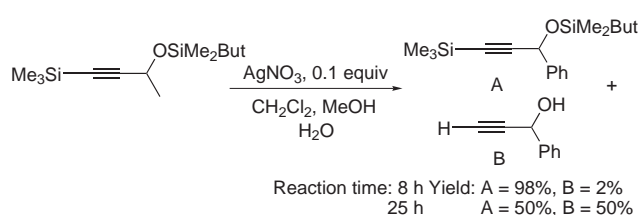
Introduction

Silver nitrate (AgNO_3 , MW 169.87) [7761-88-8] is known as lunar caustic. It is a colorless crystalline solid soluble in water. This is a versatile chemical used in pho-

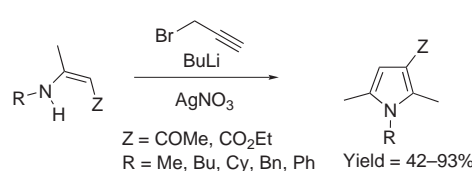
tography, silver paints, dyes, chemical analysis and gravimetric analysis. AgNO_3 is also used in pharmaceutical preparations, i.e. in eye lotions and for the treatment of gonorrhoea. It is prepared by reacting silver with nitric acid and is purified by recrystallization.

Abstract

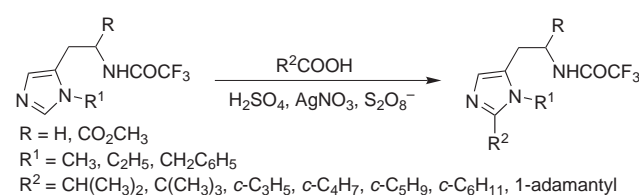
(A) Silver nitrate acts as a catalyst that selectively facilitates the deprotection of trimethylsilylacetylenes under ambient conditions. Reactions are usually carried out in a homogeneous mixture of dichloromethane, water and methanol (7:1:4), to enhance the solubility of the intermediates formed during the organic transformation. Acetal, ester, benzyl and most important other silyl groups are perfectly compatible with the reaction conditions.¹



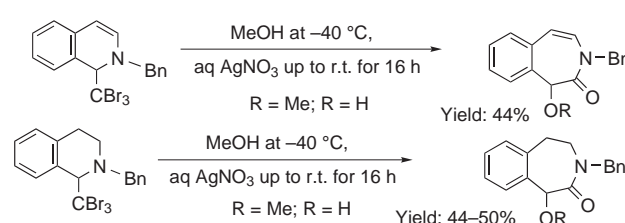
(B) Silver nitrate mediated synthesis of pyrroles is carried out in one pot by reacting secondary vinylogous amides or carbonates with propargyl bromide. This reaction, although facile, does not generate good yields.^{2,3} It has been observed that functionalized pyrroles can be efficiently prepared using a two-step sequence, by propargylation of secondary enaminones using *n*-BuLi and propargyl bromide, followed by intramolecular hydroamination catalyzed by silver nitrate.⁴



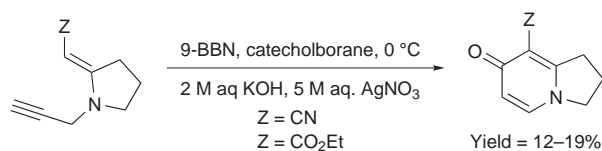
(C) Homolytic alkylation of heteroaromatic bases, i.e. substituted histidine and histamine, is carried out with the help of silver nitrate, where silver-catalyzed oxidative decarboxylation of acids by peroxydisulfate takes place. The carboxylic acid acts as a source of alkyl radical, which leads to the formation of 2,3-disubstituted L-histidine methyl ester and α -N-trifluoroacetylhistamine.^{5,6}



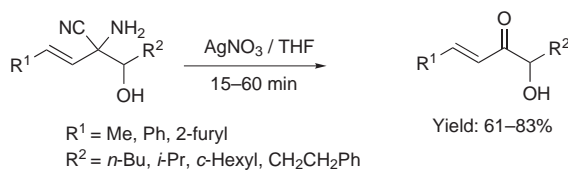
(D) In a single step, silver nitrate helps in the ring enlargement of the 1-(tribromomethyl)-1,2-dihydro- and 1-(tribromomethyl)-1,2,3,4-tetrahydroisoquinoline derivatives to 1,2-dihydro- and 1,2,3,4-tetrahydrobenzo[d]azepin-2-ones, respectively, in moderate yields. Here the silver ion acts as an electrophile, which facilitates the formation of the transient aziridinium ring. The aziridinium ring is opened by the methanol and the intermediate formed undergoes hydrolysis to give the desired product.⁷



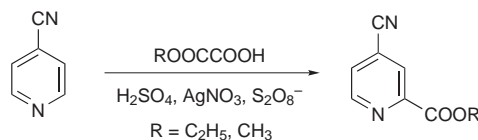
(E) Alkaline silver nitrate assists in the formation of the intramolecular coupling reaction of hydroborated products formed by addition of 9-BBN and catecholborane to C–C double and triple bonds, respectively.⁸



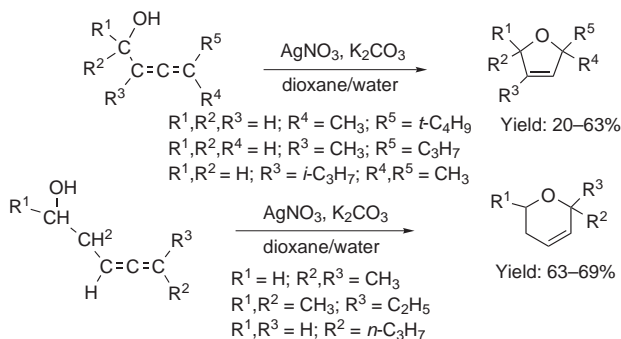
(F) Silver nitrate assists in the conversion of aminonitrile to ketones by mild hydrolysis. In this reaction, when aqueous silver nitrate solution is added to the aminonitrile dissolved in the THF solution, rapid formation of the dark gray silver nitrate precipitate takes place and with acidic workup, one the desired product is obtained.⁹



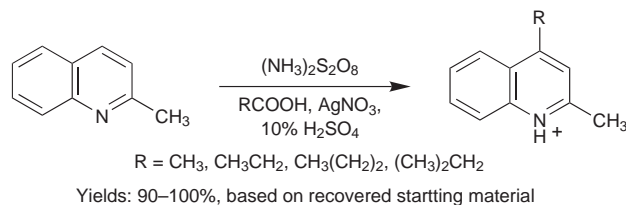
(G) The direct introduction of a carboxyl group onto a heteroaromatic base in a single step is a very useful reaction in organic synthesis. Alkoxy-carboxylation of heteroaromatic bases is carried out by silver-catalyzed decarboxylation of methyl and ethyl monoesters of oxalic acid by $S_2O_8^{2-}$. This reaction is a biphasic reaction, where monoesters are present in organic layers and protonated base is present in aqueous layer.¹⁰



(H) Silver nitrate catalyzes the cyclization of the allenic alcohols to form 2,5-dihydrofurans and 5,6-dihydro-2H-pyrans. To a solution of calcium carbonate and δ -monoalkyl, δ,δ -dialkyl substituted α -allenic alcohol, silver nitrate in water–dioxane or water–acetone is added to afford 2,5-dihydrofurans in 20–63% yields. Similarly, β -allenic alcohols are converted to the corresponding 5,6-dihydro-2H-pyrans under the same reaction conditions in moderate yields.¹¹



(I) Homolytic alkylation of heteroaromatic bases such as quinoline is catalyzed by silver nitrate, where silver-catalyzed oxidative decarboxylation of acids by peroxydisulfate is used as a source of alkyl radical. Here, the free alkyl radical acts as a nucleophile, which attacks the protonated bases; high yields and selectivities are obtained with this reaction.^{12–14}



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