SYNLETT Spotlight 259

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

Nitrosobenzene

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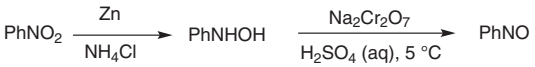
Introduction

Nitrosobenzene is a reagent used in many asymmetric syntheses with amazing results. It acts as an electrophile in catalytic enantioselective carbon–nitrogen and carbon–oxygen bond-forming reactions. It has received attention in recent years because of its high reactivity and regio- and stereoselectivities. In the presence of Lewis or Brønsted acid catalysts, enantioselective nitroso aldol or nitroso Diels–Alder reactions proceed under smooth conditions.[1] Nitrosobenzene can be used in the aminoxylation of aldehydes and ketones, and the products are precursors of 1,2-amino alcohols, terminal diols[2] and allylic alcohols.[3] It can also be used in asymmetric desymmetrization of α-hydroxy ketones.[4] Others applications are described below. This reagent is stable, inexpensive and commercially available, all of which corroborate its use.

Preparation

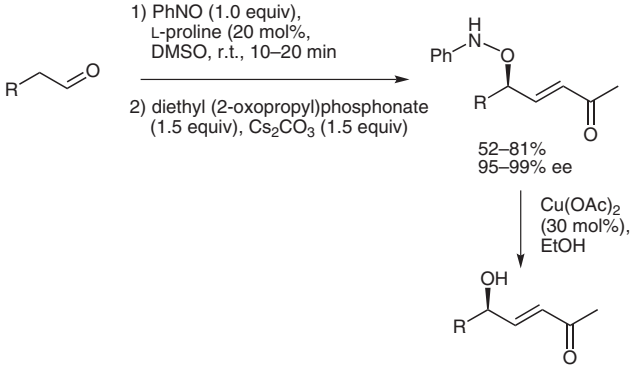
Nitrosobenzene can be prepared by the oxidation of α-phenylhydroxylamine, which is prepared by the reduction of nitrobenzene using ammonium chloride and zinc dust (Equation 1).[5]



Equation 1

Abstracts

(A) Nitrosobenzene was used in the aminoxylation of a series of aldehydes, using L-proline as catalyst. The product was easily transformed, without isolation, into the corresponding amino-substituted alcohol with addition of diethyl (2-oxopropyl)phosphonate and cesium carbonate. The yield ranged from 52 to 81% with an enantiomeric excess above 95%. Removal of the phenylamino group was achieved using $Cu(OAc)_2$, which gave the allylic alcohol.[3]



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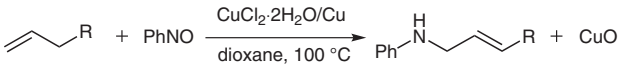
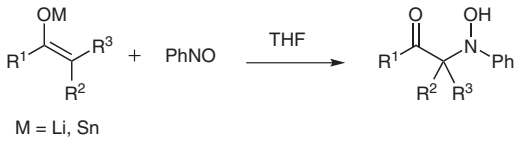
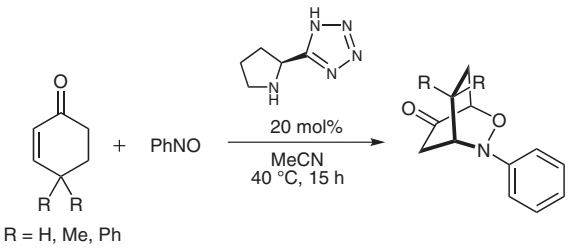
(B) Addition of nitrosobenzene to a dioxane solution (100 °C) in an excess of olefin, $CuCl_2 \cdot H_2O$ and Cu powder produces the corresponding *N*-aryl-*N*-allylamines in moderate to good yield. The Alkenes reacted with high regioselectivity with functionalization at the less substituted vinylic carbon.[6]



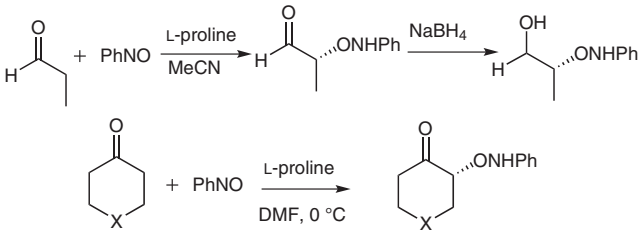
(C) Yamamoto and co-workers reported the reaction of lithium and tin enolates with nitrosobenzene. The nitroso aldol reactions proceeded smoothly to generate the N-adduct in high yield. A variety of ketones and one ester lithium enolate afforded the α-hydroxyamino product; the yields ranged from 42 to 93% and the reactions took no longer than one hour. The reaction of nitrosobenzene with tin enolates proceeded in THF at –20 °C for two hours with yields that ranged from 88 to 98% with exclusive N-selectivity.[7]



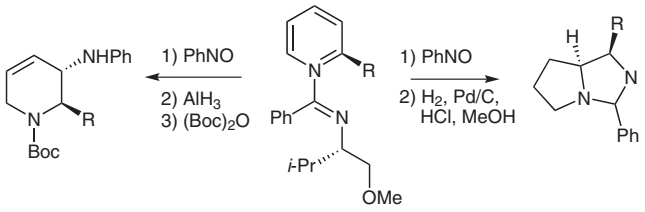
(D) Nitrosobenzene reactions with cyclohexenones in the presence of a pyrrolidine-based tetrazole catalyst afforded the cyclized Diels–Alder adduct cleanly with high enantioselectivity and moderate to good yields. Cycloheptenone was also tested and the desired product was obtained using proline catalyst.[8]



(E) Hayashi and co-workers recently reported the direct proline-catalyzed asymmetric aminoxylation of aldehydes and ketones using nitrobenzene as an oxygen source. The optimal conditions were established for both aldehydes and ketones. The yields obtained from aldehydes were good with an enantiomeric excess above 97%. Enantiomeric excess was above 96% for all the ketones tested. Both 3- and 4-substituted cyclohexanones gave the corresponding products with low diastereoselectivity but high enantioselectivity.[9]



(F) A stereoselective synthesis of *trans*-2-substituted 3-amino-2,3,6-trihydropyridines can be achieved by cycloaddition of nitrosobenzene with 2-substituted 1,2-dihydropyridines followed by chemoselective reduction of cycloadducts. In situ hydrogenation of these cycloadducts over palladium in a solution of hydrogen chloride in methanol led to tetrahydropyrroloimidazoles.[10]



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