SYNLETT
Spotlight 188

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

Sodium Azide (NaN_3): A Versatile Reagent in Organic Synthesis

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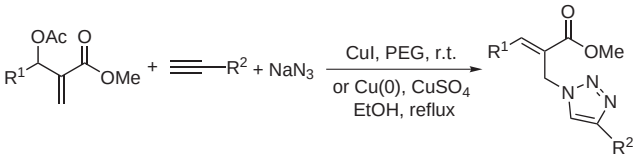
Introduction

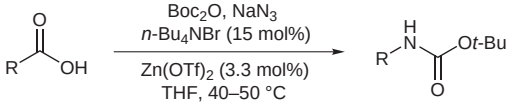
Sodium azide is a colorless, odorless, white crystalline solid, which is commercially available and widely used in industry, agriculture, medical practice, and organic transformations. It has been used for synthesis of β- and γ-azidoarylketones,[1] dialkylcarbamoyl azides,[2] diphenylphosphoryl azides,[3] acyl azides,[4] aryl azides,[5] allyl azides,[6] 1,5-fused tetrazoles,[7] 5-substituted 1*H*-tetrazoles,[8] 1,2,3-triazoles,[9] 1-aryl 1,2,3-triazoles,[10] 1,4-disubstituted 1,2,3-triazoles,[11] and 1-*N*-glycosylthiomethyl-1,2,3-triazoles.[12] In addition, sodium azide has been widely employed for preparation of α-azidoketones,[13] 1-aryl-1*H*-benzotriazoles,[14] 3-cyanoindoles,[15] and Fmoc-protected amino alcohols,[16] as a suitable nucleophile for the Michael-induced ring closure of 2-bromoalkylidenemalonates to 3,3-dialkyl-2-azidocyclopropane-1,1-dicarboxylates.[17]

Abstracts

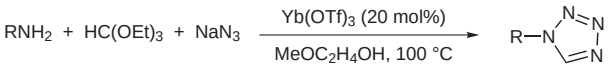
(A) Sreedhar et al. have developed an efficient method for the regioselective synthesis of 1,4-disubstituted 1,2,3-triazoles from a variety of Baylis–Hillman acetates and terminal alkynes with sodium azide using CuI as a catalyst in PEG-400 at room temperature.[18a] This one-pot reaction has also been performed in ethanol using a catalytic amount of copper turnings and copper sulfate solution.[18b]



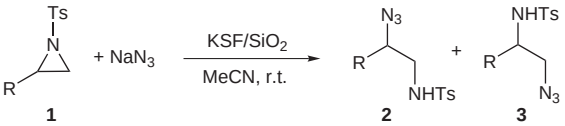
(B) A simple and efficient process for the direct conversion of carboxylic acids into carbamates has been demonstrated via Curtius rearrangement. The use of a mixture of di-*tert*-butyl dicarbonate and sodium azide allows the transformation of aliphatic carboxylic acids into alkyl azides, which rearrange to produce the corresponding isocyanates. Trapping of the isocyanates in the reaction mixture led to the desired carbamates in high yields.[19]



(C) Very recently, an efficient and convenient method has been developed for the synthesis of 1-substituted 1*H*-1,2,3,4-tetrazole compounds from amines, triethyl orthoformate and sodium azide catalyzed by $Yb(OTf)_3$.[20]



(D) A regioselective ring opening of aziridines with sodium azide can be carried out at room temperature using montmorillonite KSF/SiO_2 as promoter. Aryl aziridines underwent cleavage in a regioselective manner with preferential attack at the benzylic position to give products **2**. Alkyl-substituted terminal aziridines gave the ring-opened products **3** resulting from terminal attack of NaN_3.[21]



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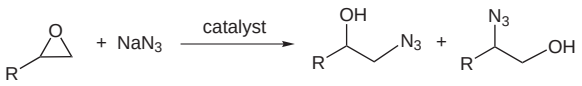
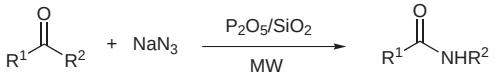
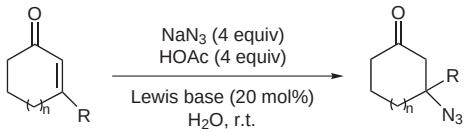
(E) The simple and most straightforward synthetic method for the preparation of 2-azidoalcohols involves the regioselective ring opening of oxiranes with sodium azide. This reaction can be carried out in the presence of Lewis acids[22] or in ionic liquids–H_2O systems.[23]



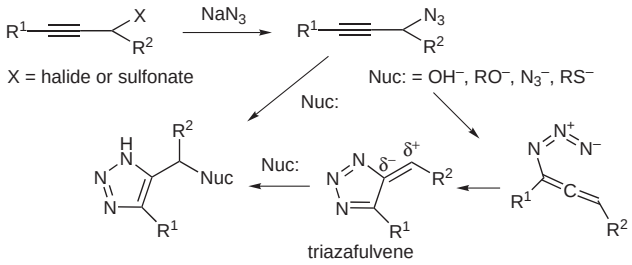
(F) A facile and efficient method for the synthesis of amides from ketones and sodium azide via Schmidt reaction using P_2O_5/SiO_2 under solvent-free microwave irradiation has been developed.[24]



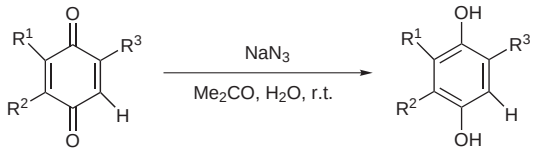
(G) Sodium azide has been used as the direct azide source in an easy and convenient synthesis of β-azidocarbonyl compounds in water.[25]



(H) Sharpless and co-workers have reported a two-step protocol for the synthesis of a series of polyfunctional N*H*-1,2,3-triazoles.[26] Propargyl azides, prepared in situ from propargyl halides or sulfonates with sodium azide, underwent a thermal rearrangement sequence to triazafulvene intermediates, which were readily captured by diverse nucleophiles.



(I) Sodium azide has also been used as a reductant for reduction of 1,4-benzoquinones to hydroquinones under neutral conditions in the presence of water.[27]



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