SYNLETT
Spotlight 234

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

p-Nitrobenzenesulfonamide

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Introduction

p-Nitrobenzenesulfonamide (*p*-NsNH_2, nosyl amide, **1**) is a valuable reagent in organic synthesis. It can be prepared from the corresponding sulfonyl chloride by treatment with either ammonium carbonate[1] or ammonia.[2] Furthermore, **1** is commercially available.

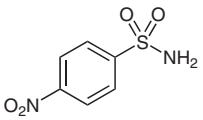

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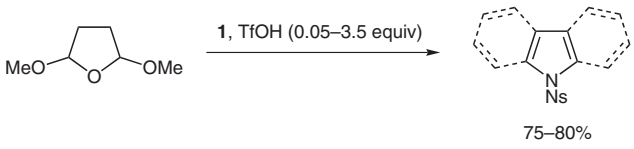
Figure 1

Sulfonamide **1** acts as a protecting and activating group in the synthesis of secondary amines.[3] The nosyl moiety can be easily removed with thiolate reagents.

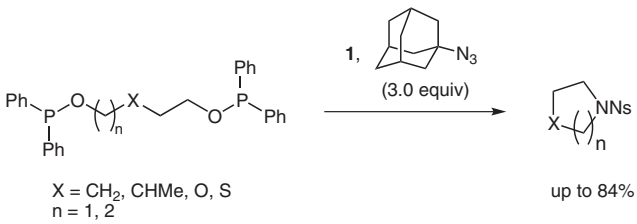
Manifold organic transformations with **1** are known in the literature. The reagent is mostly used as a source of nitrogen, for example in the assembly of heterocycles,[4,5] in imination reactions,[6] in olefin hydroamination reactions,[7] and in the C–H amination of unactivated alkanes.[8,9] Furthermore, allylic and homoallylic sulfonamides are accessible via ring-opening of methylene cyclopropenes.[10] Nitrenes generated from **1** add to olefins, thereby furnishing aziridines.[11,12] Highly enantioselective aza-Baylis–Hillman reactions were described with imines derived from **1** under organocatalytic conditions,[13] and a *p*-NsNH_2 derived dendritic catalyst proved effective in asymmetric aldol reactions.[14]

Abstracts

(A) *p*-Nitrobenzenesulfonamide (**1**) acts as a nitrogen source in the synthesis of heterocycles. Pyrroles, indoles, and carbazoles are accessible through successive annelation reactions with triflic acid.[4] Török and co-workers found that the ratio of triflic acid to reagent determines the reaction outcome. Hence, *p*-Ns pyrrole is formed with 0.05 equiv of triflic acid whereas the indole derivative is formed with an equimolar amount of the acid. An excess of triflic acid (3.5 equiv) leads to the carbazole product.



(B) Furthermore, **1** is a useful reagent in the assembly of non-aromatic heterocycles. Mukaiyama et al.[5] described an efficient method for the preparation of pyrrolidines, piperidines, morpholines, and thiomorpholines. The products were formed in moderate to good yields.



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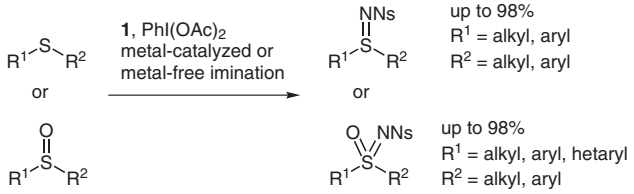
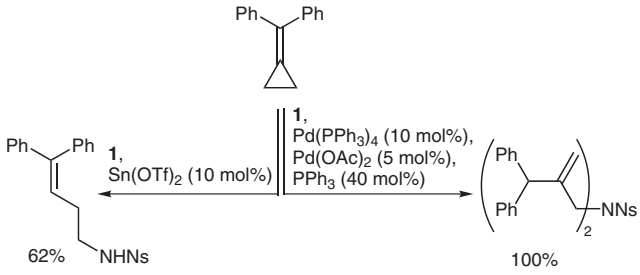
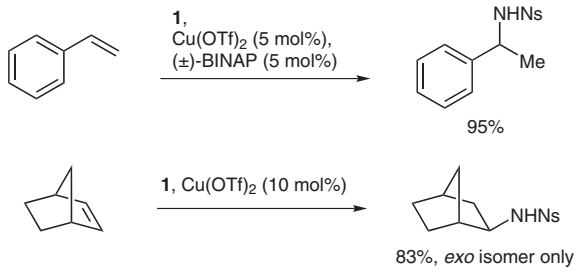
(C) Bolm and co-workers described efficient imination reactions of sulfides and sulfoxides using **1** as a nitrogen source, furnishing synthetically valuable sulfinimines and sulfoximines, respectively, in high yields. Both metal-catalyzed (Rh, Ag, Cu, Fe)[6a–d] and metal-free variants of the reaction have been reported.[6e]



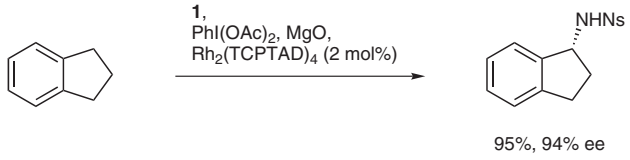
(D) Metal-catalyzed ring-opening reactions of methylene cyclopropenes with **1** were reported by Shi and co-workers. Depending on the metal catalyst used, the products of these transformations are either homoallylic[10a] or allylic[10b] sulfonamides. The latter can be deprotected to the corresponding allylic amines, which constitute interesting synthetic intermediates.



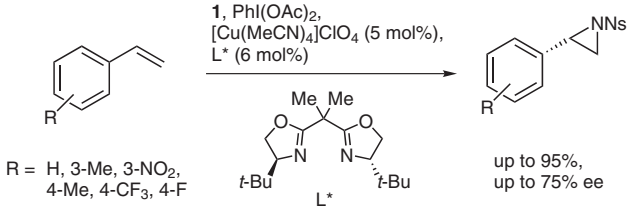
(E) Taylor et al. reported a copper-catalyzed intermolecular hydroamination of olefins with sulfonamide **1**.[7] The hydroamination of styrene furnished 1-phenethylnosylamide in excellent yield. The reaction was found to be greatly enhanced by the addition of BINAP as a ligand as it was assumed that the ligand lowered the energy barrier of the process. The protocol was also found suitable for other alkenes such as norbornene. As with the styrenic substrates, the corresponding amine was formed in good yield. Interestingly, formation of the *exo* isomer was exclusively observed in this case.



(F) Reddy and Davies achieved C–H activation reactions of alkanes with **1** and an adamantane-derived rhodium catalyst [Rh_2(TCPTAD)$_4$]. Both excellent yields and enantioselectivities in the C–H amination of indene were reported.[8]



(G) A copper-catalyzed one-pot procedure for aziridinations was recently reported by Kwong et al.[11] They used either **1** in combination with an oxidant [PhI(OAc)$_2$] or the corresponding preformed iminoiodinane [synthesized from **1** and PhI(OAc)$_2$] as nitrene source for the aziridination of styrene and derivatives thereof. In combination with Evans' oxazoline ligand, very high yields and good enantioselectivities could be obtained.



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