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Synthesis and Reactivity of Sulfamoyl Azides and 1-Sulfamoyl-1,2,3-triazoles

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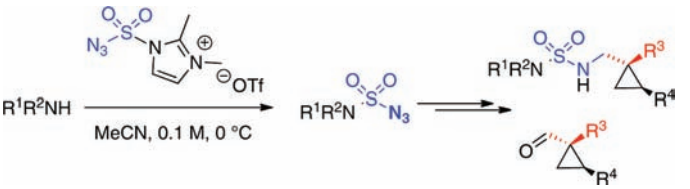
ABSTRACT



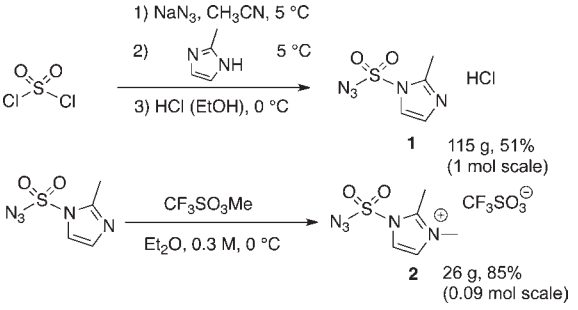
Sulfamoyl azides are readily generated from secondary amines and a novel sulfonyl azide transfer agent, 2,3-dimethyl-1*H*-imidazolium triflate. They react with alkynes in the presence of a CuTC catalyst forming 1-sulfamoyl-1,2,3-triazoles. The latter are shelf-stable progenitors of rhodium azavinyl carbenes, versatile reactive intermediates that, among other reactions, readily and asymmetrically add to olefins.

Sulfamoyl azides make only a fleeting appearance in organic synthesis. Their first preparation from sulfamoyl chlorides and sodium azide was reported in 1956 by American Cyanamid chemists.[1] However, this generally reliable route fails when preparation of arylsulfamoyl azides is attempted due to the undesired chlorination of the aromatic ring by sulfuryl chloride. Shozda and Vernon,[2] and later Griffiths,[3] developed an alternative synthesis of arylsulfamoyl azides using chlorosulfonyl azide. While this method circumvented the problem of ring chlorination, the chlorosulfonyl azide reagent was highly explosive and difficult to handle. Furthermore, the yields were modest at best, remaining generally in the 15−50% range.

Recently, imidazole-1-sulfonyl azide hydrochloride was shown to be an efficient and convenient diazo transfer reagent.[4] During our investigations, we found that alkylation of the imidazole nitrogen eliminated its diazo transfer reactivity and instead led to the transfer of the sulfonyl azide group. In this study, we introduce the imidazolium salt **2** as a novel and efficient sulfonyl azide transfer reagent.

The 2-methylated derivative **1** was prepared using a slight modification of the method developed by Goddard-Borger and Sticks for the synthesis of imidazole-1-sulfonyl azide hydrochloride.[4] The added methyl group at C-2 of the imidazole ring improves the solubility of this derivative in organic solvents[5] and is also expected to increase its stability. The free base of the imidazole **1** was efficiently alkylated with methyl triflate. The product was isolated as a crystalline solid, yielding the imidazolium sulfonyl azide transfer reagent **2** in high yield and purity (Scheme 1). Reagent **2** is a stable solid that can be stored refrigerated at 0−4 °C for at least three months without detectable decomposition.

Scheme 1. Synthesis of the Sulfonyl Azide Transfer Reagent



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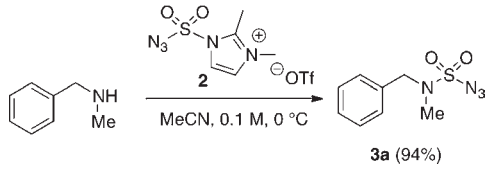
Conditions for the transfer reaction of the sulfonyl azide group to secondary amines were next investigated using *N*-methylbenzylamine as a model substrate to yield *N*-benzyl-*N*-methyl-sulfamoyl azide **3a** (Table 1). Similar group transfers that rely on sulfuryl imidazolium salts call for the inclusion of a superstoichiometric organic base.[4] In our experience, the addition of an organic base rapidly decomposed the imidazolium transfer agent and led to low yields or no product formation altogether. In the absence of an exogenous base, the sulfonyl azide transfer reaction proceeded smoothly at low temperature in polar aprotic solvents. Interestingly, yields were inversely related to the amount of **2** used in the reaction: the highest yields were observed with 1 equiv of the transfer agent, indicating that the azide product was degraded by reagent **2**.

Table 1. Optimization of Sulfamoyl Azide Transfer[a]

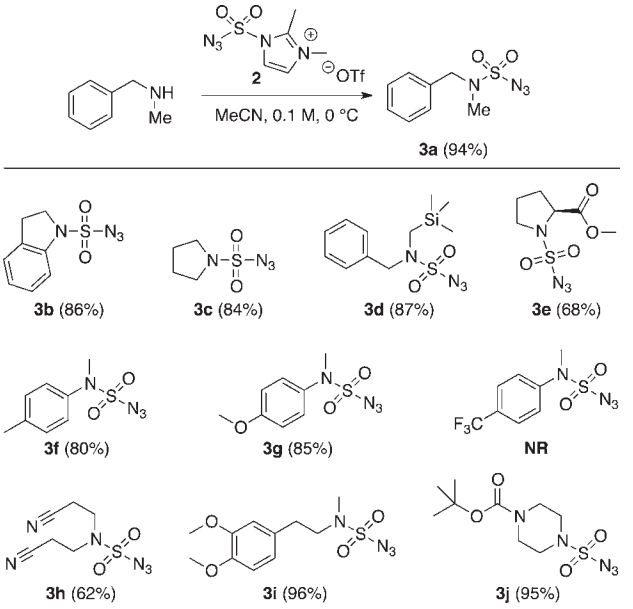


entry	solvent	concn, M[b]	*t*, °C	equiv of **2**	yield, %[c]
1	THF	0.2	25	1	84
2	THF	0.2	25	2	80
3	THF	0.2	25	3	76
4	THF	0.2	25	4	72
5	THF	0.05	25	1	90
6	THF	0.1	25	1	86
7	THF	0.2	25	1	84
8	THF	0.4	25	1	79
9	THF	0.8	25	1	75
10	dioxane	0.05	25	1	85
11	CH_2Cl_2	0.05	25	1	88
12	THF	0.05	25	1	89
13	EtOAc	0.05	25	1	98
14	MeCN	0.05	25	1	99
15	THF	0.2	0	1	96

[a] 0.5 mmol of *N*-methylbenzylamine was added neat to a stirred solution (suspension in the case of entry 4) of **2**. [b] *N*-Methylbenzylamine. [c] Yields were determined by LC-MS by linear regression using authentic **3a**, after 1.5 h.

Under these optimized conditions (CH_3CN, 0 °C, 0.1 M) sulfamoyl azides **3a**–**j** were synthesized and isolated in high yields from a variety of secondary amines (Scheme 2). The exclusive use of secondary amines is necessary to prevent hydrolysis of the sulfamoyl azide product due to *N*-H proton abstraction, which leads to the corresponding sulfamic and hydrazoic acids.[6] Isolation of the sulfamoyl azides by filtration through a short plug of silica proved to be a simple and efficient purification step due to the complete consumption of amine and the polarity difference of side products.

Scheme 2. Synthesis of Sulfamoyl Azides from 2° Amines[a]



[a] NR = no product was isolated.

Sulfamoyl azides **3a**–**d,f** were subjected to the copper-catalyzed azide–alkyne cycloaddition reaction utilizing copper(I) thiophene-2-carboxylate (CuTC) in dry toluene.[7] As expected, the use of copper sulfate and sodium ascorbate under aqueous conditions led to the formation of *N*-acylsulfamoyl containing compounds, as was previously demonstrated with sulfonyl azides.[8] Sulfamoyl triazoles **4a**–**d,f** were synthesized in high yield and isolated as solids or oils following an aqueous ammonium hydroxide work-up (Scheme 3).

Sulfamoyl triazoles are generally more hydrolytically stable as compared to the sulfonyl triazoles congeners. Thus, after three days in 0.5 M sodium hydroxide in acetonitrile/water, triazole **4a** displayed only minor degradation to the *N*H-triazole, with an estimated 80% of **4a** remaining intact. Conversely, in 0.5 M hydrochloric acid in acetonitrile/water, triazole **4a** showed significant degradation with an estimated 33% of **4a** remaining after three days. Under neutral acetonitrile/water conditions no degradation was detected over a two week period.

Reactions of azavinyl carbenes[9] obtained from sulfamoyl triazoles were next examined. In the presence of a chiral rhodium(II) catalyst, sulfamoyl triazole **4a** smoothly

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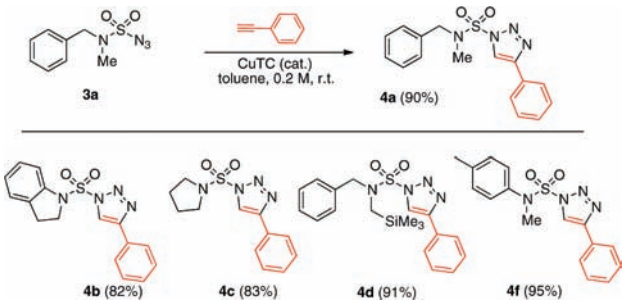
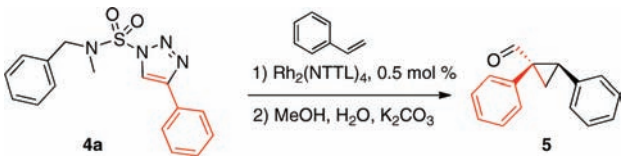
Scheme 3. Synthesis of Sulfamoyl Triazoles[a]



[a] Isolated yields after column chromatography reported in parentheses.

cyclopropanated styrene. Optimal conditions for cyclopropanation with catalytic $Rh_2(S\text{-NTTL})_4$ were determined based on GC-MS and chiral HPLC analysis of the isolated aldehyde **5**, (the hydrolysis product of the sulfamoyl imine produced during cyclopropanation, Table 2).[9]

Table 2. Asymmetric Cyclopropanation with Sulfamoyl Triazoles[a]

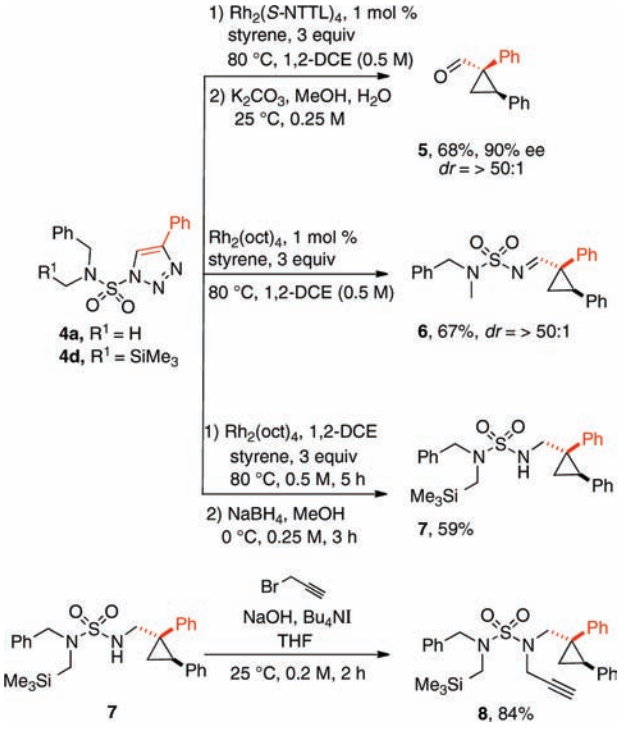


entry	solvent	*t*, °C	*dr* (trans:cis)[b]	ee, %[c]	yield, %[d]
1	1,2-DCE	65	3:1	88[e]	30
2	1,2-DCE	80	50:1	90	80
3	1,1,2,2-TCE	100	25:1	89	60
4	$CHCl_3$	80	>50:1	94	63
5	**Toluene**	**80**	**>50:1**	**90**	**79**

[a] Reactions consisted of 0.5 mmol triazole **4a**, $Rh_2(S\text{-NTTL})_4$ (1 mol %), Styrene (3.0 equiv). [b] Determined by GC/MS. [c] *Trans* diastereomer, determined by chiral HPLC. [d] Isolated yield of **5**.

In contrast to the relatively unstable sulfonyl imines produced by the reaction of sulfonyl triazoles and olefins in the presence of rhodium(II) catalysts, we were able to isolate sulfamoyl imine **6** in a high yield as a stable solid following silica gel chromatography (Scheme 4). Alternatively, the sulfamoyl imine could be efficiently reduced with sodium borohydride to yield sulfamoyl amine **7**, which can be further functionalized via simple transformations. For example, a propargyl group was easily introduced under trivial conditions, producing the propargyl amine derivative **8** in a high yield (Scheme 4).

Scheme 4. Transformations of Sulfamoyl Triazoles



As described in this report, the readily available and stable imidazolium reagent is immediately useful in synthesis. It efficiently converts secondary amines to alkyl- and arylsulfamoyl azides, which readily participate in copper-catalyzed azide–alkyne cycloadditions providing sulfamoyl triazoles. These sulfamoyl triazoles retain many of the properties of the sulfonyl congeners and engage in the rhodium-catalyzed cyclopropanation with olefins, while offering the increased stability of both starting materials and imine products.

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Supporting Information Available. Experimental procedures and full spectroscopic data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.