Convenient One-Pot Synthesis of Sulfonyl Azides from Sulfonic Acids

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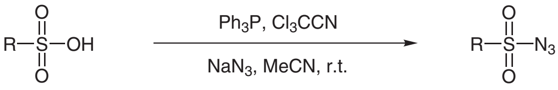
Abstract: We have developed a one-pot process for preparing sulfonyl azides by treating sulfonic acids with trichloroacetonitrile, triphenylphosphine, and sodium azide at room temperature. A wide range of sulfonyl azides was synthesized in excellent yields under mild conditions.

Key words: sulfonic acid, sulfonyl azide, trichloroacetonitrile, triphenylphosphine, sodium azide

Sulfonyl azides are versatile reagents for a variety of chemical transformations. They have been used as valuable reagents for the preparation of α-diazocarbonyl reagents,[1] the hydroazidation of olefins,[2] the aziridation of olefins,[3] the radical amination,[4] and metal-catalyzed coupling reactions.[5] Owing to a wide range of applications, a general and convenient access to sulfonyl azides is highly desirable.

The most practical laboratory method for preparing sulfonyl azides involves the reaction of sulfonyl chlorides with azides.[6] The reaction requires the availability of sulfonyl chlorides, which are troublesome to prepare and handle. Generally, sulfonyl chlorides are prepared by treating sulfonic acids with chlorinating agents such as $SOCl_2$,[7] $POCl_2$,[8] PCl_5,[9] triphosgene,[10] and cyanuric chloride.[11] These methods have some drawbacks including low yields of the desired product, using a large excess of highly toxic chlorinating agents, and producing corrosive byproducts. Alternatively, sulfonyl azides were prepared by reacting sulfonyl anhydrides,[12] α-disulfones,[13] or 1-sulfonylbenzotriazole[14] with sodium azide. These methods suffer from difficulty in preparing the starting materials. Thus, there is a great demand for the development of convenient synthetic methods towards assessing sulfonyl azides.

It has been reported that the combination of trichloroacetonitrile and triphenylphosphine is efficient for chlorinating carboxylic acids and sulfonic acids under mild conditions.[15] We envisioned that the combination of trichloroacetonitrile and triphenylphosphine might provide a general protocol for preparing various sulfonyl azides from sulfonic acids. We herein report a mild and efficient procedure for the synthesis of sulfonyl azides from sulfonic acids with trichloroacetonitrile, triphenylphosphine, and sodium azide (Scheme 1).



Scheme 1

We chose *p*-toluenesulfonic acid, which was dehydrated by azeotropic distillation in benzene, as model substrate to achieve optimal reaction conditions. Treating a solution of *p*-toluenesulfonic acid (1 equiv), Ph_3P (1 equiv), and NaN_3 (1 equiv) with Cl_3CCN (1 equiv) in MeCN at room temperature afforded sulfonyl azide in poor yield (Table 1, entry 1). However, when the amount of Cl_3CCN and Ph_3P was increased, the yield of sulfonyl azide increased up to 92% (entry 3). An increase of the amount of NaN_3 made the required reaction time shorten (entry 4). High reaction temperature caused a loss in the yield of sulfonyl azide with forming a nonpolar side product (entry 5). A large excess of trichloroacetonitrile and triphenylphosphine was not efficient to improve the yield of sulfonyl azide (entry 6). We examined the reactivity of some reagents to find suitable halogenating agents for preparing sulfonyl chlorides such as $Cl_3CCOCCl_3$, Cl_3CCO_2Et, Br_3CCO_2Et, and Cl_3CCONH_2 (entries 7–13). Trichloroacetonitrile is the choice of halogenating reagents.

To investigate the generality and scope of the reaction, various aryl and alkyl sulfonic acids were subjected to the reaction conditions. Table 2 presents the results. All aryl and aliphatic sulfonic acids gave excellent yields of sulfonyl azides. Aryl sulfonic acids afforded somewhat higher yields of sulfonyl azides than aliphatic sulfonic acids. Aryl sulfonic acids with an electron-rich benzene ring appear to be more reactive, giving higher yields of product. Aryl sulfonic acids with an electron-poor benzene ring afforded slightly lower yields of sulfonyl azides. The relative reactivity of aromatic sulfonic acids is consistent with a mechanism involving attack on the sulfur atom of sulfonyl group by a nucleophilic agent.

In summary, we developed a one-pot process for preparing sulfonyl azides from sulfonic acids with Cl_3CCN, Ph_3P, and NaN_3. The reaction provides convenience, efficiency, and generality for the preparation of sulfonyl azides from various sufonic acids. Employing less toxic reagents make this process attractive from the standpoint of environment.

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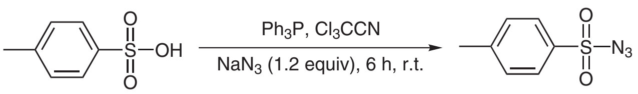
Table 1 Reaction of *p*-Toluenesulfonic Acid with Cl_3CCN, Ph_3P, and NaN_3

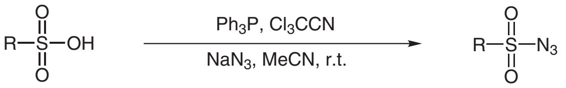


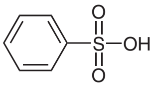
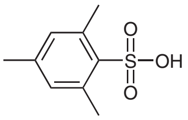
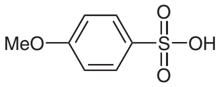
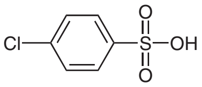
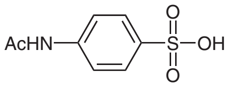
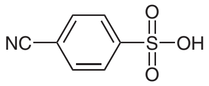
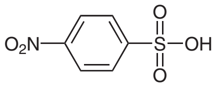
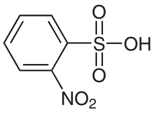
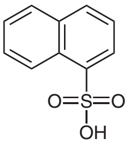
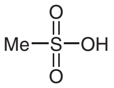
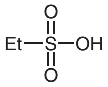
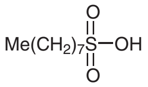
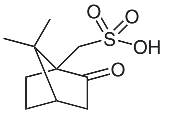
Entry	Ph_3P (equiv)	Halogenating agent (equiv)	Isolated yield (%)
1	1	Cl_3CCN (1)	38
2	1	Cl_3CCN (2)	41
3	2	Cl_3CCN (2)	92
4[a]	2	Cl_3CCN (2)	95
5[b]	2	Cl_3CCN (2)	71
6	3	Cl_3CCN (3)	87
7	2	CCl_4 (2)	trace
8	2	$Cl_3CCOCCl_3$ (2)	31
9[b]	2	$Cl_3CCOCCl_3$ (2)	35
10	3	$Cl_3CCOCCl_3$ (3)	33
11	2	Cl_3CCO_2Et (2)	18
12	2	Br_3CCO_2Et (2)	11
13	2	Cl_3CCONH_2 (2)	12

[a] Conditions: NaN_3 (2.4 equiv), 3 h.

[b] At reflux.

Table 2 Synthesis of Various Sulfonyl Azides from Sulfonic Acids[a]



Entry	Sulfonic acid	Time (h)	Yield of RSO_2N_3 (%)
1		0.5	94
2		0.5	93
3		0.5	89
4		0.5	97
5		0.5	90
6		0.5	91
7		2	82
8		0.5	93
9		0.5	89
10	 $\mathrm{Me{-}S(O)_2{-}OH}$	1	89
11	 $\mathrm{Et{-}S(O)_2{-}OH}$	2	83
12	 $\mathrm{Me(CH_2)_7S(O)_2{-}OH}$	2	84
13		2	86

[a] See the Typical Experimental Procedure for the reaction conditions.

Typical Experimental Procedure

A solution of PTSA (172 mg, 1.0 mmol), Ph_3P (525 mg, 2.0 mmol), Cl_3CCN (0.2 mL, 2 mmol) and NaN_3 (156 mg, 2.4 mmol) in MeCN (3 mL) was stirred at r.t. for 3 h. The mixture was diluted with CH_2Cl_2 (10 mL) and washed with H_2O (3 mL). The organic layer was dried over anhyd $MgSO_4$. After filtration the solvent was removed, and the residue was purified with column chromatography on SiO_2 (hexanes–EtOAc, 20:1) to give *p*-toluenesulfonyl azide [186 mg, 95%; mp 23–25 °C (Lit.[14] 22–25 °C)].

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