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# A fast and efficient method for the preparation of aryl azides using stable aryl diazonium silica sulfates under mild conditions

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ABSTRACT

An efficient, fast, and straightforward procedure for the synthesis of aromatic azides using aryl diazonium silica sulfates and sodium azide at room temperature under mild conditions is described. The use of inexpensive materials, simple and clean work-up, short reaction times and good yields are advantages of this method.



Aryl azides are versatile intermediates with various applications in organic and bioorganic chemistry.[1] A major application of these compounds is 1,3-dipolar cycloaddition to produce five-membered heterocycles.[2] In addition, aromatic azides are well known for their use as photoaffinity labeling agents for proteins.[3] Typically, these compounds are prepared from aromatic amines with nitrous acid followed by addition of sodium azide at low temperature.[1a,4] Aryl azides have also been prepared by reaction of arylmagnesium halides or aryllithium reagents with *para*-toluenesulfonyl azide.[5] The above-mentioned conversion has also been accomplished under mild conditions using a combination of aryl amine, $TfN_3$, $CuSO_4$, and triethylamine.[6] Direct coupling of aryl halides[7] or aryl boronic acids[8] with sodium azide catalyzed by copper salts has been reported. These compounds have also been synthesized from aromatic amines with *t*-BuONO followed by addition of $NaN_3$[9] or $TMSN_3$[10] under mild conditions. Furthermore, $[ArN_2][BF_4]$ salts immobilized in $[Bmim][PF_6]$ ionic liquid with $TMSN_3$ have been reported for the preparation of aryl azides.[11] Although some of these methods utilize convenient protocols with good yields, some of them suffer from disadvantages such as long reaction times, low yields, and high temperatures leading to decomposition of the aryl azides, poor stability of the reagents, use of toxic solvents, and high costs.

In continuation of our studies on the stabilization of diazonium salts on silica sulfuric acid and their applications in organic synthesis,[12] we report herein an efficient, fast, and convenient procedure for the synthesis of aryl azides employing aryl diazonium silica sulfates in the presence of sodium azide at room temperature (Scheme 1).

Diazonium salts are versatile compounds in organic chemistry. However, their poor thermal stability limits their applications. Usually these compounds are synthesized at around 10 °C, and to avoid their decomposition, they are handled below 0 °C. In our previous work,[12] we reported an efficient, fast, and convenient method for the preparation of aryldiazonium salts supported on the surface of silica sulfuric acid[13] (aryldiazonium silica sulfates). We found that these aryldiazonium salts, $ArN_2^{+-}OSO_3 - SiO_2$, were sufficiently stable and could be kept at room temperature under anhydrous conditions.[12] For example, 4-nitrophenyl diazonium silica sulfate, which had been stored in a desiccator at room temperature for three days, reacted with sodium azide in $H_2O$ and provided almost the same yield of 1-azido-4-nitrobenzene as that prepared from fresh 4-nitrophenyl diazonium silica sulfate (Table 1, entry 12). To illustrate the scope of the present method, a range of aromatic amines were rapidly converted into the corresponding aryl

$$ArN_2^{+}\,^{-}OSO_3\text{-}SiO_2 \xrightarrow[\text{r.t., 10-15 min}]{NaN_3,\ H_2O} ArN_3$$

**Scheme 1.**

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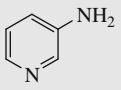
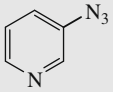
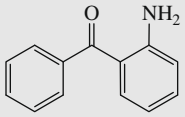
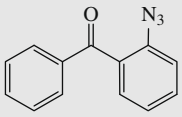
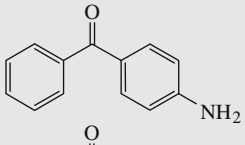
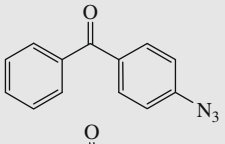
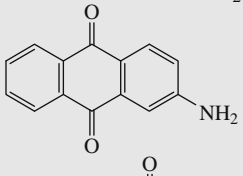
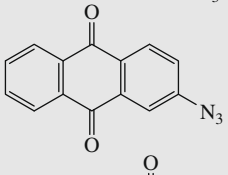
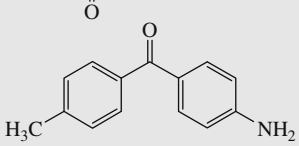
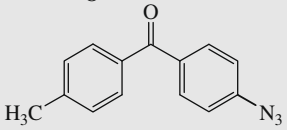
**Table 1**
Conversion of aryl amines into the corresponding aryl azides using aryldiazonium silica sulfates at room temperature[a]

| Entry | Substrate | Time (min) | Product | Yield (%) |
|---|---|---|---|---|
| 1 | $C_6H_5NH_2$ | 10 | $C_6H_5N_3$ | 77 |
| 2 | 4-$MeC_6H_4NH_2$ | 10 | 4-$MeC_6H_4N_3$ | 80 |
| 3 | 4-$MeOC_6H_4NH_2$ | 10 | 4-$MeOC_6H_4N_3$ | 78 |
| 4 | 4-$PhC_6H_4NH_2$ | 15 | 4-$PhC_6H_4N_3$ | 81 |
| 5 | 4-$ClC_6H_4NH_2$ | 10 | 4-$ClC_6H_4N_3$ | 83 |
| 6 | 3-$ClC_6H_4NH_2$ | 10 | 3-$ClC_6H_4N_3$ | 82 |
| 7 | 4-$BrC_6H_4NH_2$ | 10 | 4-$BrC_6H_4N_3$ | 84 |
| 8 | 4-$H_2NC_6H_4COOH$ | 15 | 4-$N_3C_6H_4COOH$ | 90 |
| 9 | 2-$H_2NC_6H_4COOH$ | 15 | 2-$N_3C_6H_4COOH$ | 84 |
| 10 | 4-$MeCOC_6H_4NH_2$ | 10 | 4-$MeCOC_6H_4N_3$ | 86 |
| 11 | 4-$NCC_6H_4NH_2$ | 10 | 4-$NCC_6H_4N_3$ | 85 |
| 12 | 4-$O_2NC_6H_4NH_2$ | 10 | 4-$O_2NC_6H_4N_3$ | 82 |
| 13 | 2-$O_2NC_6H_4NH_2$ | 15 | 2-$O_2NC_6H_4N_3$ | 78 |
| 14 | 3-$O_2NC_6H_4NH_2$ | 10 | 3-$O_2NC_6H_4N_3$ | 83 |
| 15 |  | 10 |  | 65 |
| 16 |  | 15 |  | 85 |
| 17 |  | 15 |  | 87 |
| 18 |  | 15 |  | 76 |
| 19 |  | 15 |  | 88 |

[a] Yield refers to isolated pure products which were characterized from their spectral data and by comparison with authentic samples.[6–11,15,18]

azides in good to high yields under mild conditions (Table 1).[14,15] In contrast to related methods, aromatic amines with electron-withdrawing groups or electron-donating groups also reacted. The steric effects of *ortho*-substituents had relatively little influence on the reaction time and yields (Table 1, entries 9, 13, and 16). The corresponding phenol derivatives were formed in trace yields as by-products. The crude products were obtained by filtration and work-up, and if necessary, were purified by short column chromatography. In contrast to conventional methods, the reaction rate increases on supporting the aryldiazonium salt on silica sulfuric acid, as the surface area for reaction increases.[12,16] Finally, after completion of the reaction and isolation of the product, the solid support could be recycled.[12] In addition, the present procedure for the preparation of aryldiazonium silica sulfates and aryl azides is safe and non-explosive because by supporting aryldiazonium salts on the surface of silica sulfuric acid as a bulky support, the stability of these salts increases.[12,17]

In summary, we have developed an efficient, rapid, experimentally simple, and environmentally benign method for the preparation of aryl azides using aryldiazonium silica sulfates. These reactions proceed at room temperature under mild conditions in high yields. Further investigations on new applications of this method are ongoing in our laboratories.

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14. *General procedure for the preparation of aryl diazonium silica sulfate:* An aromatic amine (1 mmol), silica sulfuric acid (0.70 g),[13e,f] and sodium nitrite (2 mmol) were ground in a mortar with a pestle for a few minutes to afford a homogeneous mixture. Then, a few drops of water were added gradually and the reaction mixture was ground for 10–15 min to give the corresponding aryl diazonium silica sulfate. *Typical procedure for the preparation of 1-azido-4-bromobenzene*: To a stirring solution of sodium azide (2.5 mmol, 0.163 g) in $H_2O$ (3 mL), freshly prepared 4-bromophenyldiazonium silica sulfate (1 mmol) was added gradually and the reaction mixture was stirred at rt for 10 min. The mixture was diluted with EtOAc (15 mL) and was filtered after vigorous stirring. The residue was extracted with EtOAc (3 × 12 mL) and the combined organic layer was washed with 5% NaOH solution (12 mL) and then dried over anhydrous $Na_2SO_4$. The solvent was evaporated to afford 1-azido-4-bromobenzene in 84% yield (0.165 g).
15. *(4-Azidophenyl)(4-methylphenyl)methanone* (Table 1, entry 19): pale yellow solid; mp 80–82 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.83 (2H, d, $J$ = 8.8 Hz), 7.69 (2H, d, $J$ = 8.0 Hz), 7.30 (2 H, d, $J$ = 8.0 Hz), 7.12 (2 H, d, $J$ = 8.8 Hz), 2.45 (3 H, s). $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 195.06, 144.19, 143.27, 134.85, 134.40, 132.00, 130.12, 129.06, 118.72, 21.68. IR (KBr) cm$^{-1}$: 3025, 2923, 2129, 2089, 1642, 1597, 1496, 1412, 1306, 1286, 1178, 1115, 929, 851, 826, 752. Anal. Calcd for $C_{14}H_{11}N_3O$: C, 70.88; H, 4.64; N, 17.72. Found: C, 70.75; H, 4.75; N, 17.63.
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