# Synthesis of any Initriles using the stable any I diazonium silica sulfates Davood Habibi\*, Somayyeh Heydari and Mahmoud Nasrollahzadeh

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An efficient method for preparation of aryl nitriles is reported using Cu(I) to catalyse the reaction of aryl diazonium silica sulfates with sodium cyanide under mild conditions at room temperature in water. This method has the advantages of high yields, simple methodology, short reaction times and easy work-up.

Keywords: aryl diazonium silica sulfates, sodium cyanide, aryl nitriles, Cu(I)

Nitriles are one of a number of important functional groups in organic synthesis such as esters, amides, carboxylic acids, amines and nitrogen-containing heterocycles and have been used in the construction of various pharmaceutically important compounds, agricultural chemicals and functional materials.<sup>1,2</sup> There are several methods for the synthesis of nitriles such as the dehydration of aromatic amides, the condensation of carboxylic acids, the nucleophilic substitution of alkyl halides with inorganic cyanides, the reaction of esters with Me<sub>2</sub>AlNH<sub>2</sub> and the conversion of aromatic bromides. Other procedures include oxidative conversion of amines using AgO, Pb(OAc)<sub>4</sub>, cobalt peroxide, Na<sub>2</sub>S<sub>2</sub>O<sub>8</sub> or (Bu<sub>4</sub>N)<sub>2</sub>S<sub>2</sub>O<sub>8</sub> with metals, NaOCl, K<sub>3</sub>Fe(CN)<sub>6</sub>, Cu(I) or Cu(II) with oxygen, PhIO, RuCl<sub>3</sub> and related Ru reagents and trichloroisocyanuric acid with TEMPO.<sup>3,11</sup> Also, various aromatic bromides and iodides were converted into the corresponding aryl nitriles with n-BuLi and DMF followed by the reaction with I<sub>2</sub> in aqueous NH<sub>3</sub>.<sup>12</sup> However, there are several disadvantages in the literature methods such as the use of expensive and toxic reagents, low yields, long reaction times, harsh reaction conditions, difficulty in obtaining the starting materials and tedious work-up.

Aryl diazonium salts are typically more reactive than aryl halides and have been extensively employed as nitrogencentred radical scavengers<sup>13,14</sup> and as sources of aryl radicals in the Meerwein,15 Gomberg-Bachmann,16 Pschorr,17 and Sandmeyer<sup>18</sup> type reactions. The Sandmeyer reaction has long been one of the main routes for the synthesis of aryl halides or cyanides which includes two steps: diazotisation of the corresponding amines with sodium nitrite in the presence of hydrochloric or sulfuric acid, and the subsequent reaction with cuprous halides or cyanide.<sup>3,4</sup> Despite the high yields, the utility of this method is limited due to disadvantages such as the formation of phenols in aqueous media at >10 °C, formation of azophenols by coupling of phenols with diazonium salts, the use of hydrochloric acid or sulfuric acid (hazardous, toxic, extremely corrosive and homogeneous reagent, which cannot easily be recovered), difficulties in the preparation and storage of diazonium salts (which are synthesised at around 10 °C and handled below 0 °C to avoid their decomposition), the instability and explosive nature of the diazonium salts, the evolution of poisonous gases such as hydrogen cyanide and the use of low temperatures. Recently, Beletskaya and co-workers reported the synthesis of aryl nitriles from the reaction of aryl diazonium salts with KCN in acetonitrile catalysed by CuCN/phen/Cu(BF<sub>4</sub>)<sub>2</sub>/dibenzo-18-crown-6 under an inert atmosphere.<sup>19</sup> However, it is important to note that the aryldiazonium salts bearing electron-donating groups led to the formation of corresponding nitriles in low yields. Therefore, the pursuit of more convenient and practical synthetic methods still remains an active research area.

To resolve the problem of the instability of diazonium salts and to avoid the application of hydrochloric or sulfuric acid, stable aryl diazonium salts supported on silica sulfuric acid

(SSA) were used. These are stable at room temperature and can be stored over the extended periods of time without decomposition and can be easily recycled.20

In continuation of our recent work on nitriles and the synthesis of nitrogen-containing compounds,<sup>21,25</sup> here we report a mild, efficient and convenient method for the preparation of nitriles from the reaction between aryl diazonium silica sulfates as stable reagents with NaCN catalysed by CuCN in water at room temperature (Scheme 1).

### **Results and discussion**

Initially, to determine the optimum reaction conditions, a reaction between p-nitrophenyl- diazonium silica sulfate, NaCN and CuCN was carried out and it was found that the best conditions are 1.5 mmol of NaCN, 1.0 mmol of aryl diazonium silica sulfates, 0.2 mmol of CuCN and 3.0 mL of H<sub>2</sub>O (Table 1).

The Sandmeyer cyanation of anilines having electron-donating groups was found to be difficult<sup>18</sup> and in a number of cases, no product was obtained even with the stoichiometric amounts of copper salt.26 In our method a series of anilines containing both electron-donating and electron-withdrawing groups were converted into the corresponding aryl nitriles in high yields (Table 2). Different functional groups such as alkyl, nitro and halogens remained intact during the reactions. The nature of the substituent on the aryl diazonium silica sulfate did not affect the reaction time (Table 2, entries 1-8) and the steric effects of the ortho-substituents also had no influence on the reaction time and yields as well (Table 1, entry 7). 1,4-Diaminobenzene afforded the double substitution product (Table 2, entry 8).

Due to the high surface area of the aryl diazonium silica sulfates, reactions were carried out under mild conditions,

$ArNH_2$ <u>NaNO<sub>2</sub>, wet SSA</u> $ArN_2^+$	OSO <sub>3</sub> -SiO <sub>2</sub> <u>NaCN, CuCN</u> ArCN
r.t., grinding	H <sub>2</sub> O, r.t.
10-20 min	10 m in

Scheme 1	Preparation	of nitriles.
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Table 1 Preparation of *p*-nitrobenzonitrile using varying amounts of NaCN and CuCN at room temperature<sup>a</sup>

Entry	NaCN/mmol	CuCN/mmol	Yield/% <sup>b</sup>
1	1	0	10
2	1.5	0	13
3	2.5	0	20
4	1	0.1	40
5	1.5	0.1	55
6	2.5	0.1	87
7	1.5	0.2	87
8	1.5	0.25	87

<sup>a</sup>Reaction conditions: *p*-nitrophenyl diazonium silica sulfates (1 mmol),  $H_2O$  (3 mL), reaction time (10 min). <sup>b</sup> Isolated yield.

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 Table 2
 Preparation of aryl nitriles in the presence of CuCN by reaction of aryl diazonium silica sulfate with sodium cyanide at room temperature

Entry	Substrate	Product	v/cm <sup>-1a</sup>	Yield/% <sup>b</sup>	M.p./°C (lit. <sup>ref</sup> /°C) <sup>c</sup>
1	C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub>	C₅H₅CN	2229	87	Oil <sup>27</sup>
2	p-MeC <sub>6</sub> H₄ŇH₂	p-MeC <sub>6</sub> H₄CN	2360	86	Oil <sup>27</sup>
3	p-IC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub>	ρ-IC <sub>e</sub> H <sub>4</sub> CN	2225	83	124–128 (124–128) <sup>28</sup>
4	p-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> NH <sub>2</sub>	p-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CN	2233	87	145–147 (146–148) <sup>27</sup>
5	p-OHC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub>	p-OHC <sub>6</sub> H₄CN	2234	84	111–112 (110–113)28
6	m-BrC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub>	m-BrC <sub>e</sub> H <sub>4</sub> CN	2229	85	38-40 (38-40)28
7	o-CI-p-NO <sub>2</sub> C <sub>6</sub> H <sub>3</sub> NH <sub>2</sub>	o-CI-p-NO <sub>2</sub> C <sub>6</sub> H <sub>3</sub> CN	2235	83	81–83 (commercial, 83–84)
8	p-NH <sub>2</sub> C <sub>e</sub> H <sub>4</sub> NH <sub>2</sub>	p-CNC <sub>6</sub> H <sub>4</sub> CN	2232	86	221-225 (221-225)28
9	p-OMeC <sub>6</sub> H₄NH₂	p-OMeČ <sub>6</sub> H <sub>4</sub> CN	2225	82	58-60 (60-62)27

<sup>a</sup>IR absorption of nitriles in wavenumbers (cm<sup>-1</sup>).

<sup>b</sup>Yield refers to the pure isolated product.

°The compound reported in the literature.

short reaction times and gave higher yields.<sup>20</sup> The only byproducts of these reactions are trace amounts of the corresponding phenol derivatives. The products were obtained by filtration and the subsequent extraction with ethyl acetate. In a number of cases, short column chromatography is used for the products purification and recrystallisation is not needed. The solid-supported acid can be easily recovered after completion of the reaction and isolation of the product and the diazonium salts are consumed in the reaction.

All the products are known and the spectroscopic data (FT-IR and <sup>1</sup>H NMR) and melting points were consistent with those reported in the literature. The disappearance of the two strong and sharp absorption bands (NH<sub>2</sub> stretching bands), and the appearance of a CN stretching band in the IR spectra, were evidence for the formation of aryl nitriles.

In conclusion, we have developed a highly efficient method for preparation of aryl nitriles using aryl diazonium silica sulfates with moderate to good yields. The advantages of this protocol include a simple reaction setup only at room temperature, not requiring specialised equipment, high product yields, mild conditions and short reaction times.

#### Experimental

*CAUTION:* Most solid diazonium salts in the dry state explode upon heating and shock<sup>29,30</sup> and also some reactions of aryl diazonium salts come with a serious warning of an explosion hazard.<sup>31</sup> We found that in contrast to other diazonium salts, the aryl diazonium silica sulfates were sufficiently stable to be kept at room temperature in a desiccator in a dried state.<sup>20</sup> Due care was taken below with reactions which involve the use of cyanide solutions/ mixtures and unreacted cyanide was removed.

# Synthesis of aryl diazonium silica sulfate;<sup>20</sup> general procedure

An aromatic amine (1.0 mmol), silica sulfuric acid (0.7 g) and sodium nitrite (2.0 mmol) were ground in a mortar with a pestle for a few minutes to prepare a homogeneous mixture. Then, a few drops of water were gradually added and the reaction mixture was ground for 10–15 min to give the corresponding aryl diazonium silica sulfate.

Synthesis of 1,4-dicyanobenzene (Table 2, entry 8; typical procedure 1,4-Phenylene diazonium silica sulfate (1.0 mmol) was added gradually to NaCN (1.5 mmol) and CuCN (0.2 mmol) in H<sub>2</sub>O (3.0 mL) and the reaction mixture was stirred at room temperature for 10 min. The mixture was diluted with ethyl acetate (20 mL), filtered after vigorous stirring and extracted with ethyl acetate (3×15 mL). The combined organic layers were washed with 5% NaOH solution (10 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated to give the pure product in 86% yield (entry 8). The inorganic phase was washed with 10% ferrous sulfate solution (3×15 mL) to remove any unreacted cyanide ions.<sup>32</sup>

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