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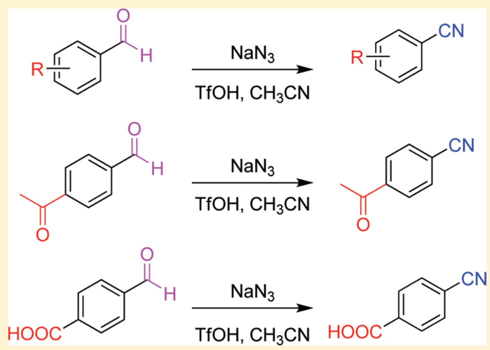
Chemoselective Schmidt Reaction Mediated by Triflic Acid: Selective Synthesis of Nitriles from Aldehydes

Balaji V. Rokade and Kandikere Ramaiah Prabhu*

Department of Organic Chemistry, Indian Institute of Science, Bangalore 560 012, Karnataka, India

Supporting Information

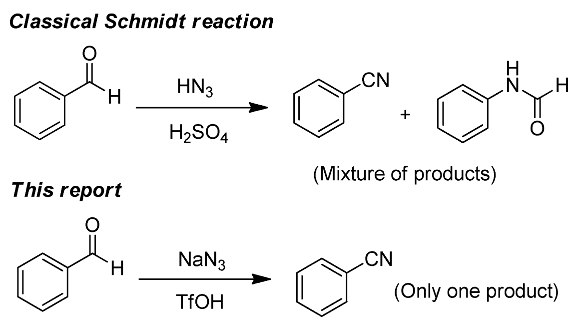
ABSTRACT: An excellent utility of Schmidt reaction of aldehydes to access corresponding nitriles in an instantaneous reaction is demonstrated. The reaction of aldehydes with NaN_3 and TfOH furnishes the corresponding nitriles in near quantitative yields and tolerates a variety of electron-withdrawing and electron-donating substituents on the substrates. Formanilides, a common side product in Schmidt reaction, is not observed in this reaction. Besides these advantages, the salient feature of this reaction is that it exhibits a remarkable chemoselectivity, as acid and ketone functionalities are well tolerated under the reaction conditions. The reaction is easily scalable, high yielding, and nearly instantaneous.



■ INTRODUCTION

The Schmidt reaction of carbonyl compounds is a well addressed reaction.[1] It is well-known that under the Schmidt reaction conditions, ketones and carboxylic acids are converted into their corresponding amides[2] and amines[3] respectively, whereas aldehydes furnish a mixture of formanilides and nitriles.[4] Therefore, there is a great surge in the utility and applications of Schmidt reactions of ketones[2] and acids,[3] while Schmidt reactions of aldehydes are limited because of the formation of mixtures of corresponding formanilides and nitriles (Scheme 1).[4] Interestingly, pioneering work of Aubé on intramolecular Schmidt reaction of carbonyl compounds, particularly ketones, with alkyl azides unraveled excellent methods to accomplish amides, lactams, oxazolines, and their application to synthesize natural products.[5] Addition of azides to olefins in the presence of Bronsted acid to activate olefin to get aziridines is also reported.[6] In this context, in 1952 McEwen et al. revealed that in the Schmidt reaction of aldehyde with HN_3, the product ratio of nitrile to formanilide depends upon the amount of sulfuric acid employed in the reaction.[4] Besides this report, to the best of our knowledge, utility of Schmidt reaction for selective transformation of aldehyde to one of the two possible products in Schmidt reaction is scarce.[7] Hence, it is desirable to develop a method to access either nitrile or formanilide selectively using Schmidt reaction protocol.

Scheme 1



Nitriles are important structural motifs in organic synthesis,[8a−g] which are valuable intermediates that are easily amenable to their corresponding acids, esters, amines, amides, aldehydes, benzamidines, and nitrogen-containing heterocycles.[8h,i] In continuation of our work to develop simple synthetic strategies to accomplish nitriles,[9] in this paper we present an efficient utility of the Schmidt reaction for a selective transformation of aldehydes to their nitriles using triflic acid (TfOH) (Scheme 1).

■ RESULTS AND DISCUSSION

We began the current study by employing 4-nitrobenzaldehyde **1a** and a variety of Bronsted acids. A number of Bronsted acids were screened to optimize the reaction conditions by reacting 4-nitrobenzaldehyde **1a** and NaN_3 (Table 1). The reactions were performed using several acids (3 equiv) such as acetic acid, methanesulfonic acid, *p*-toluenesulfonic acid (*p*-TSA), sulfuric acid, and trifluoroacetic acid (TFA) (Table 1, entries 2−6) in CH_3CN at room temperature. As can be seen in Table 1, most these reactions failed to produce the expected product even after prolonged reaction (24 h), and the starting material was intact. Interestingly, perchloric acid ($HClO_4$) in a reaction with aldehyde **1a** and NaN_3 (1.5 equiv) furnished the corresponding nitrile **2a** in low yield (6%, 24 h, Table 1, entry 7). Although this reaction has produced a low yield of the nitrile, it furnished only the corresponding nitrile, and the formation of formanilide was not observed. Further, this

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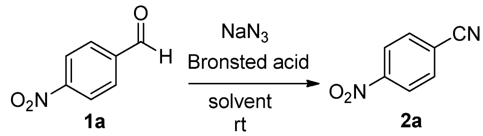
Table 1. Optimization of Reaction Conditions[a]



entry	Bronsted acid	solvent	yield (%)[b]
1	none	CH_3CN	nr
2	AcOH	CH_3CN	nr
3	CH_3SO_3H	CH_3CN	nr
4	*p*-TSA	CH_3CN	nr
5	H_2SO_4	CH_3CN	nr
6	TFA	CH_3CN	nr
7	$HClO_4$ (70%)	CH_3CN	6
8	TfOH	CH_3CN	99[c]
9	TfOH	CH_3CN	6[d]
10	TfOH	CH_3CN	66[e]
11	TfOH	THF	nr
12	TfOH	$CHCl_3$	21
13	TfOH	CH_2Cl_2	nr
14	TfOH	DMF	nr
15	TfOH	Et_2O	nr
16	TfOH	EtOAc	75
17	TfOH	toluene	nr
18	TfOH	MeOH	nr

[a]Reactions were performed with **1a** (1 mmol), NaN_3 (1.5 mmol), and Bronsted acid (3 mmol), solvent (2 mL) for 24 h at room temperature. [b]Refers to ^1H NMR yield. nr = no reaction. [c]Reaction completed in 2 min. [d]TfOH (1.5 equiv). [e]TfOH (2 equiv).

reaction indicated that it is necessary to use stronger Bronsted acids to achieve the better results such as $HClO_4$ (Table 1, entry 7). Encouraged by the outcome, a reaction of **1a** and NaN_3 using TfOH was performed. In this reaction, it was pleasing to find that 4-nitrobenzonitrile **2a** was formed, almost instantaneously, in near quantitative yield (99%, Table 1, entry 8), and side products were not observed even in trace amounts.[4] It is worthwhile to note that the similar reaction of *p*-nitrobenzaldehyde, H_2SO_4, and NaN_3 in benzene resulted in the formation of a mixture of corresponding nitrile and formanilide.[4] On the basis of these inputs, further screening studies were carried out using **1a** as a precursor. Decreasing the amount of TfOH to 1.5 or 2 equiv resulted in the formation of the product in low yield (6 and 66% respectively, Table 1, entries 9−10). Solvent screening studies revealed that solvents such as $CHCl_3$ or EtOAc are not suitable for this reaction, as the reactions in these solvents have produced a mixture of products along with unreacted starting material. Similarly, the reaction in diethyl ether, CH_2Cl_2, THF, toluene, and DMF did not proceed, as the starting material was recovered unaltered. Further, MeOH as a solvent resulted in the formation of corresponding dimethyl acetal as the product.[10] Nevertheless, the most satisfactory results were obtained by using CH_3CN as solvent.[11] Although CH_3CN is known to react with TfOH, it is used as solvent in several organic reactions.[12] Therefore, we carried out further reactions with NaN_3 (1.5 equiv), TfOH (3 equiv) using CH_3CN as solvent at room temperature.

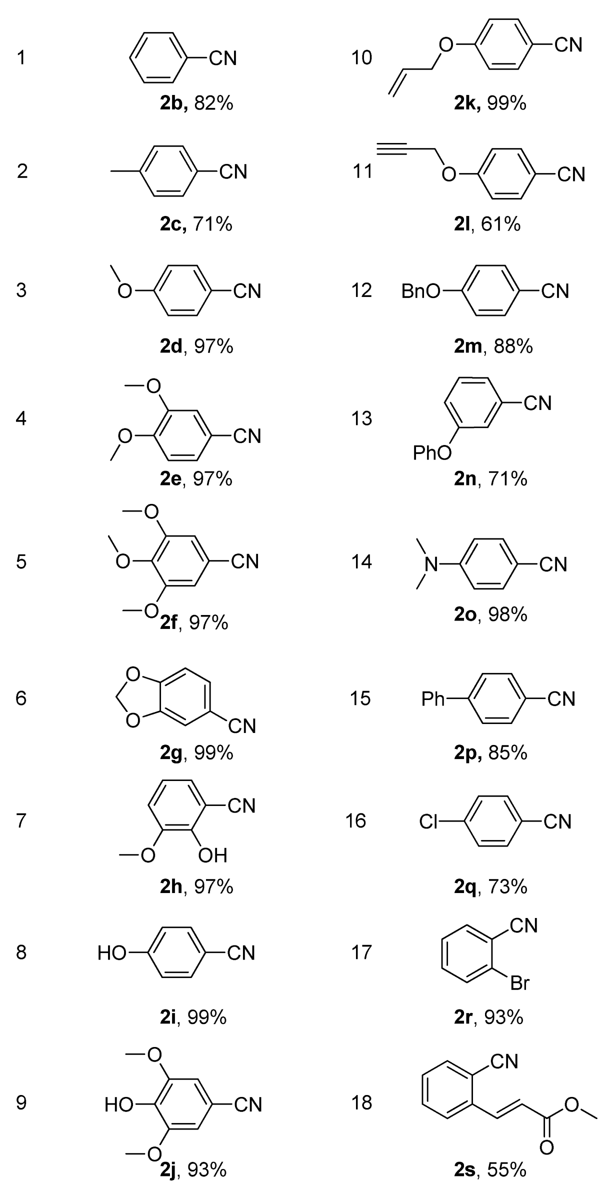
With the optimized reaction conditions, we explored the scope and limitation of the reaction with a variety of aldehydes, and results are compiled in Table 2. In general, it was noticed that under the optimal conditions, a variety of aldehydes were converted into their corresponding nitriles in good to excellent yields without forming other regiomer, *N*-substituted formamides (Table 2). Benzaldehydes bearing electron-donating and electron-withdrawing groups underwent smooth conversion to furnish their corresponding nitriles regioselectively in good to excellent yields (Table 2, entries 1−22). Benzaldehyde reacted smoothly to furnish benzonitrile in 82% (Table 2, entry 1). Similarly, benzaldehyde substituted with a variety of substituents such as alkyl, methoxy, hydroxyl, allyloxy, propargyloxy, benzyloxy, phenyl, halo, amide, ester, and nitro groups underwent a facile reaction to produce corresponding nitriles in excellent yields (Table 2). Furthermore, it was found that the methodology is general and works well with cinnamaldehyde to furnish the corresponding cinnamonitrile in excellent yield (Table 2, entry 23). Similarly, *p*-nitrocinnamaldehyde and *p*-methoxycinnamaldehyde reacted smoothly to furnish their corresponding nitriles **3b** and **3c** in almost quantitative yields (Table 2, entries 24−25). Alicyclic α,β-unsaturated aldehyde, 2-bromocyclohex-1-enecarbaldehyde, reacted smoothly under the standard reaction conditions to furnish the nitrile, 2-bromocyclohex-1-enecarbonitrile, **3d** in 60% yield (Table 2, entry 26). In most of the reactions, the product obtained was NMR pure; therefore, further purification was not necessary.

After successful attempts to convert benzyl and cinnamyl aldehydes to their corresponding nitriles, we attempted selective reaction of aldehydes in the presence of ketone and acid functionalities, hoping that ketone or carboxylic acid groups would be inert under the reaction conditions. It is well-known that aryl ketones and acids undergo a facile Schmidt reaction to furnish their corresponding amides[2] and amines,[3] respectively, which have been well exploited in organic synthesis. To test this hypothesis, 4-acetylbenzaldehyde was subjected to standard reaction conditions to obtain the corresponding 4-acetylbenzonitrile **2x** in almost quantitative yield (98%, Scheme 2). Similarly, 4-formylbenzoic acid under the similar reaction conditions furnished the corresponding 4-formylbenzonitrile **2y** in 99% yield (Scheme 2). The selectivity observed in the formation of nitrile in the presence of keto- and carboxylic functionality was further confirmed by performing an intermolecular reaction of a mixture of 4-methoxybenzaldehyde and 4-methoxyacetophenone. As expected, 4-methoxybenzaldehyde reacted to yield the corresponding nitrile **2d** (99%), whereas 4-methoxyacetophenone was intact during the reaction condition (Scheme 3). Similarly, under the similar reaction conditions, an intermolecular reaction of 4-methoxybenzaldehyde and 4-methoxybenzoic acid resulted in the formation of 4-methoxybenzonitrile **2d** in almost quantitative yield (99%), while 4-methoxybenzoic acid was intact during the reaction conditions (Scheme 3). These reactions reiterate that the Schmidt reaction using TfOH is selective for the transformation of aldehydes to their nitriles in the presence of ketones or carboxylic acid functionalities (Schemes 2 and 3).

To examine the application of this methodology in large scale, the reaction of **1a** was carried out in 10 mmol scale. As expected, the product **2a** was obtained in 95% yield after purification (Scheme 4), which is comparable to the yield obtained in small-scale reaction (1 mmol, entry 8, Table 1).

We believe that the selective formation of nitriles from the corresponding aldehyde goes through the expected pathway of Schmidt reaction. Hydazoic acid attacks the aldehyde to form the corresponding azido alcohol, which loses water to furnish the intermediate **I**. Further, the intermediate **I** loses nitrogen to afford the corresponding nitrile (Scheme 5). It appears that

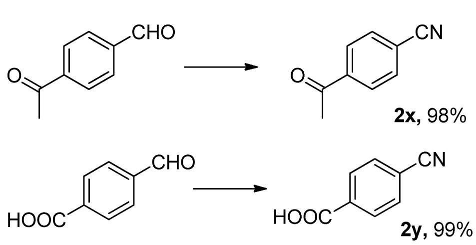
Table 2. Substrate Scope for Schmidt Reaction[a,b]



[a]Reaction conditions: aldehyde (1 mmol), NaN_3 (1.5 mmol), TfOH (3 mmol), CH_3CN (2 mL) at rt for 2 min. [b]Isolated yields.

migration of hydrogen atom is preferred over phenyl group migration and has no other preferences, as substrates with electron-withdrawing or electron-donating groups are undergoing a facile reaction under the reaction conditions to furnish the corresponding nitrile as the sole product. The plausible mechanism of this reaction is shown in Scheme 5, wherein TfOH first reacts with NaN_3 to form HN_3, which further reacts with aldehyde in the presence of TfOH followed by dehydration to form intermediate **I**, which yields nitrile.[13]

Scheme 2. Intramolecular Chemoselective Transformation of Aldehyde to Nitrile[a]



[a]Reaction conditions: **1a** (1 mmol), NaN_3, (1.5 mmol), TfOH (3 mmol), CH_3CN (2 mL) at rt for 2 min.

■ CONCLUSION

In conclusion, we have shown an excellent utility of Schmidt reaction of aldehydes to obtain corresponding nitriles. This reaction is almost instantaneous and furnishes the corresponding nitriles in near quantitative yields and tolerates electron-withdrawing and electron-donating substituents. Additionally, side product formanilide is not observed. Besides these advantages, the salient feature of this reaction is the remarkable selectivity seen in the reaction of aldehyde functionality in the presence of carboxylic acid and ketone functionalities under the reaction conditions. Further work to explore the scope of this reaction is underway in our laboratory.

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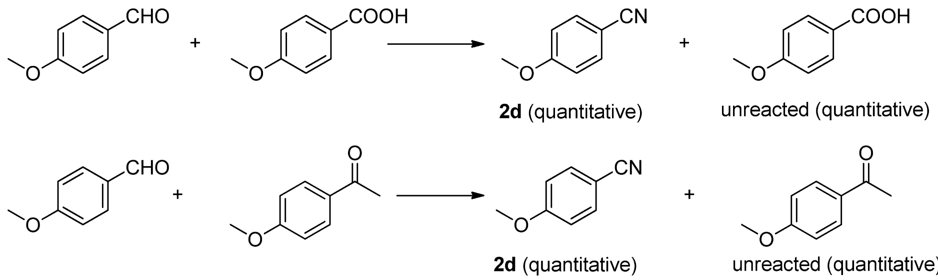
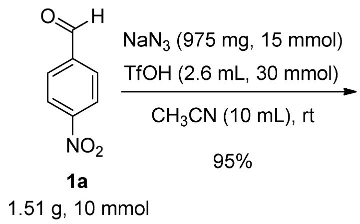
Scheme 3. Intermolecular Chemoselective Transformation of Aldehyde to Nitrile[a]



[a]Reaction conditions: **1a** (1 mmol), NaN_3, (1.5 mmol), TfOH (3 mmol), CH_3CN (2 mL) at rt for 2 min

Scheme 4. Scaling-up Experiment



■ EXPERIMENTAL SECTION

General Experimental Methods. NMR spectra were recorded on in $CDCl_3$; tetramethylsilane (TMS; δ = 0.00 ppm) served as internal standards for ^{1}H NMR; chemical shifts (δ) are reported in ppm relative to TMS. The corresponding residual nondeuterated solvent signal ($CDCl_3$: δ = 77.00 ppm) was used as internal standards for ^{13}C NMR. High-resolution mass spectra were obtained using a TOF spectrometer using simultaneous electrospray (ESI). Column chromatography was conducted on silica gel 230−400 mesh (Merck), and preparative thin-layer chromatography was carried out using silica gel GF-254.

Typical Experimental Procedure, Synthesis of Nitriles from Aldehydes. Triflic acid (3 mmol) was added to a well-stirred solution of aldehyde (1 mmol), sodium azide (1.5 mmol) in CH_3CN (2 mL), and the mixture was stirred at room temperature until the reaction was completed (monitored by TLC, ∼ 2 min.). After removal of the solvent under reduced pressure, the residue was extracted with EtOAc (3 × 15 mL), and the combined organic extract was washed with water, dried over anhydrous Na_2SO_4, and purified by silica gel column (in most of the reactions, the product obtained was NMR pure; further purification was not necessary).

4-Nitrobenzonitrile (2a).[14] Prepared as described in the general experimental procedure. White solid: yield 99% (146.5 mg); mp 148−149 °C (lit.[9a] 148−149 °C); R_f (25% EtOAc/hexane) 0.5; IR (KBr, cm^{-1}) 2222; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J = 8.9 Hz, 2H), 7.90 (d, J = 8.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.0, 133.4, 124.2, 118.3, 116.8; MS (m/z) 148 (M$^+$).

Benzonitrile (2b).[9a] Prepared as described in the general experimental procedure. Colorless liquid: yield 82% (84.4 mg); R_f (10% EtOAc/hexane) 0.80; IR (Neat, cm^{-1}) 2225; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66−7.59 (m, 3H), 7.49−7.45 (m, 2H); ^{13} C NMR (100 MHz, $CDCl_3$) δ 132.7, 132.0, 129.0, 118.8, 112.3.

4-Methylbenzonitrile (2c). Prepared as described in the general experimental procedure. White solid: yield 71% (83.0 mg); mp 27−29 °C (lit.[15] 26−28 °C); R_f (15% EtOAc/hexane) 0.7; IR (KBr, cm^{-1}) 2226; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 8 Hz, 2H), 7.27 (d, J = 8.4 Hz, 2H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.6, 132.0, 129.8, 119.1, 109.2, 21.8; HRESI-MS (m/z) Calculated for C_8H_7N (M + H) 118.0657, found (M + H) 118.0654.

4-Methoxybenzonitrile (2d). Prepared as described in the general experimental procedure. Colorless solid: yield 97% (129.0 mg); mp 55−57 °C (lit.[9b] 56−57 °C); R_f (25% EtOAc/hexane) 0.50; IR (KBr, cm^{-1}) 2218; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 8.4 Hz, 2H), 6.94 (d, J = 8.0 Hz, 2H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 133.8, 119.1, 114.6, 103.8, 55.4; HRESI-MS (m/z) Calculated for C_8H_7NO (M + Na) 156.0425, found (M + Na) 156.0427.

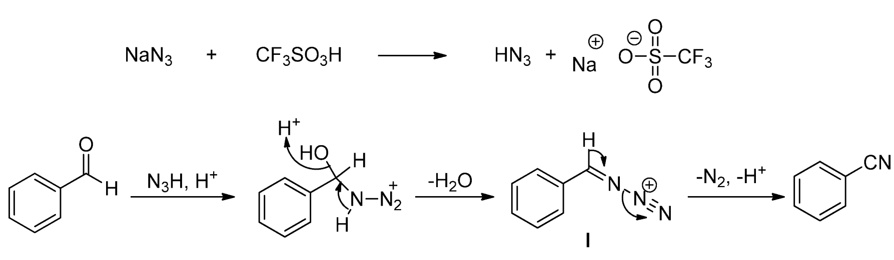
3,4-Dimethoxybenzonitrile (2e). Prepared as described in the general experimental procedure. Colorless solid: yield 97% (158.1 mg); mp 63−65 °C (lit.[9b] 65−66 °C); R_f (25% EtOAc/hexane) 0.50; IR (KBr, cm^{-1}) 2223; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, J = 8.4 Hz, 1H), 7.08 (s, 1H), 6.91 (d, J = 8.4 Hz, 1H), 3.94 (s, 3H), 3.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.8, 149.1, 126.4, 119.2, 113.8, 111.1, 103.8, 56.1, 56.0; HRESI-MS (m/z) Calculated for $C_9H_9NO_2$ (M + Na) 186.0531, found (M + Na) 186.0533.

3,4,5-Trimethoxybenzonitrile (2f). Prepared as described in the general experimental procedure. Colorless solid: yield 97% (187.2 mg); mp 93−95 °C (lit.[9b] 92−94 °C); R_f (25% EtOAc/hexane) 0.50; IR (KBr, cm^{-1}) 2226; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.87 (s, 2H), 3.90 (s, 3H), 3.88 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.5, 142.3, 118.9, 109.4, 106.7, 61.0, 56.3; HRESI-MS (m/z) Calculated for $C_{10}H_{11}NO_3$ (M + Na) 216.0637, found (M + Na) 216.0637.

1,3-Benzodioxole-5-carbonitrile (2g). Prepared as described in the general experimental procedure. White solid: yield 99% (145.5 mg); mp 83−85 °C (lit.[9b] 90−93 °C); R_f (15% EtOAc/hexane) 0.8; IR (KBr, cm^{-1}) 2223; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, J = 8.0 Hz, 1H), 7.03 (s, 1H), 6.86 (d, J = 8.0 Hz, 1H), 6.07 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 148.0, 128.2, 118.8, 111.3, 109.1, 104.9, 102.2; HRESI-MS (m/z) Calculated for $C_8H_5NO_2$ (M + Na) 170.0218, found (M + Na) 170.0218.

2-Hydroxy-3-methoxybenzonitrile (2h). Prepared as described in the general experimental procedure. Solid: yield 97% (144.5 mg);

Scheme 5. Plausible Mechanism



mp 55–57 °C (lit.[16] 56–57 °C); R_f (15% EtOAc/hexane) 0.6; IR (KBr, cm^{-1}) 2220; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (s, 1H), 7.30–7.21 (m, 2H), 6.99 (s, 1H), 4.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.9, 146.3, 144.5, 124.9, 123.1, 113.3, 111.0, 56.3; HRESI-MS (m/z) Calculated for $C_8H_7NO_2$ (M + H) 150.0555 found (M + H) 150.0550.

4-Hydroxybenzonitrile (2i). Prepared as described in the general experimental procedure. Solid: yield 99% (117.8 mg); mp 108–110 °C (lit.[17] 107–109 °C); R_f (15% EtOAc/hexane) 0.65; IR (KBr, cm^{-1}) 2233; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 8.8 Hz, 2H); 6.94 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 134.3, 119.3, 116.5, 102.5; HRESI-MS (m/z) Calculated for C_7H_5NO (M + H) 120.0449 found (M + H) 120.0452.

4-Hydroxy-3,5-dimethoxybenzonitrile (2j). Prepared as described in the general experimental procedure. Solid: yield 93% (166.4 mg); mp 105–106 °C (lit.[18] 107–109 °C); R_f (15% EtOAc/hexane) 0.6; IR (KBr, cm^{-1}) 2226; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.87 (s, 2H), 6.02 (s, 1H), 3.92 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.1, 139.3, 119.3, 109.2, 102.2, 56.5; HRESI-MS (m/z) Calculated for $C_9H_9NO_3$ (M + Na) 202.0480 found (M + Na) 202.0480.

4-(Prop-2-en-1-yloxy)benzonitrile (2k). Prepared as described in the general experimental procedure. Colorless solid: yield 99% (157.4 mg); mp 43–46 °C (lit.[9c] 43–44 °C); R_f (25% EtOAc/hexane) 0.5; IR (KBr, cm^{-1}) 2218; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 8.8 Hz, 2H), 6.96 (d, J = 8.8 Hz, 2H), 6.08–5.98 (m, 1H), 5.42 (d, J = 17.2 Hz, 1H), 5.33 (d, J = 10.4 Hz, 1H), 4.59 (dd, J_1 = 0.8 Hz, J_2 = 5.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8, 133.9, 132.0, 119.1, 118.4, 115.4, 104.0, 68.9; HRESI-MS (m/z) Calculated for $C_{10}H_9NO$ (M + Na) 182.0582, found (M + Na) 182.0580.

4-(Prop-2-yn-1-yloxy)benzonitrile (2l). Prepared as described in the general experimental procedure. White solid: yield 61% (95.7 mg); mp 109–111 °C (lit.[9c] 113–114 °C); R_f (15% EtOAc/hexane) 0.4; IR (KBr, cm^{-1}) 2222; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 8.8 Hz, 2H), 7.04 (d, J = 8.8 Hz, 2H), 4.75 (d, J = 2.0 Hz, 2H), 2.57 (t, J = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 133.9, 118.9, 115.6, 104.9, 76.7, 76.5, 55.9; HRESI-MS (m/z) Calculated for $C_{10}H_7NO$ (M + Na) 180.0425, found (M + Na) 180.0425.

4-(Phenylmethyl)benzonitrile (2m). Prepared as described in the general experimental procedure. Colorless solid: yield 88% (183.9 mg); mp 93–95 °C (lit.[9c] 94–96 °C); R_f (25% EtOAc/hexane) 0.5; IR (KBr, cm^{-1}) 2217 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 8.8 Hz, 2H), 7.41–7.35 (m, 5H), 7.01 (d, J = 8.8 Hz, 2H), 5.11 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9, 135.6, 134.0, 128.7, 128.4, 127.4, 119.1, 115.5, 104.1, 70.2; HRESI-MS (m/z) Calculated for $C_{14}H_{11}NO$ (M + Na) 232.0738, found (M + Na) 232.0736.

3-Phenoxybenzonitrile (2n).[19] Prepared as described in the general experimental procedure. Purified on a silica gel column (EtOAc/hexane, 10:90). Light yellow oil: yield 71% (138.4 mg); R_f (15% EtOAc/hexane) 0.75; IR (Neat, cm^{-1}) 2232 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.34 (m, 4H), 7.25–7.18 (m, 3H), 7.02 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1, 155.4, 130.6, 130.2, 126.3, 124.7, 122.7, 121.0, 119.7, 118.3, 113.4; HRESI-MS (m/z) Calculated for $C_{13}H_9NO$ (M + Na) 218.0582, found (M + Na) 218.0581.

4-(*N*,*N*-Dimethylamino)benzonitrile (2o). Prepared as described in the general experimental procedure. Solid: yield 98% (143.0 mg); mp 73–75 °C (lit.[20] 74–75 °C); R_f (15% EtOAc/hexane) 0.6; IR (KBr, cm^{-1}) 2211; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 9.2, 2H), 6.64 (d, J = 9.2 Hz, 2H), 3.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.4, 133.3, 120.7, 111.3, 97.3, 39.9; HRESI-MS (m/z) Calculated for $C_9H_{10}N_2$ (M + Na) 169.0742 found (M + Na) 169.0745.

4-Phenylbenzonitrile (2p). Prepared as described in the general experimental procedure. White solid: yield 85% (152.1 mg); mp 82–83 °C (lit.[21] 83–84 °C); R_f (15% EtOAc/hexane) 0.7; IR (KBr, cm^{-1}) 2226; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73–7.66 (m, 4H), 7.58 (d, J = 7.2 Hz, 2H), 7.50–7.40 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.6, 139.1, 132.5, 129.0, 128.6, 127.7, 127.2, 118.9, 110.8; HRESI-MS (m/z) Calculated for $C_{13}H_9N$ (M + Na) 202.0633, found (M + Na) 202.0632.

4-Chlorobenzonitrile (2q). Prepared as described in the general experimental procedure. Purified on a silica gel column (EtOAc/hexane, 6:94). White solid: yield 73% (100.0 mg); mp 91–92 °C (lit.[22] 90–92 °C); R_f (15% EtOAc/hexane) 0.7; IR (KBr, cm^{-1}) 2226 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 8.8 Hz, 2H), 7.47 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.5, 133.3, 129.7, 117.9, 110.8; MS (m/z) 137.

2-Bromobenzonitrile (2r). Prepared as described in the general experimental procedure. Solid: yield 93% (169.2 mg); mp 52–55 °C (lit.[22] 53–54 °C); R_f (25% EtOAc/hexane) 0.6; IR (KBr, cm^{-1}) 2225; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70–7.66 (m, 2H), 7.49–7.41 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.3, 133.8, 133.2, 127.6, 125.3, 117.1, 115.9; MS (m/z) 183 (M + H).

(*E*)-Methyl 3-(2-Cyanophenyl)prop-2-enoate (2s). Prepared as described in the general experimental procedure. White solid: yield 55% (102.8 mg); mp 94–96 °C (lit.[23] 94 °C); R_f (25% EtOAc/hexane) 0.5; IR (KBr, cm^{-1}) 2223; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 16.0 Hz, 1H), 7.72 (t, J = 8.0 Hz, 2H), 7.63 (t, J = 7.6 Hz, 1H), 7.48 (t, J = 7.6 Hz, 1H), 6.61 (d, J = 16.0 Hz, 1H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 139.6, 137.3, 133.5, 132.9, 130.1, 126.9, 122.6, 117.1, 112.7, 52.0; HRESI-MS (m/z) Calculated for $C_{11}H_9NO_2$ (M + Na) 210.0531 found (M + Na) 210.0533.

4-Cyano-*N*,*N*-diethylbenzamide (2t). Prepared as described in the general experimental procedure. Purified on a silica gel column (EtOAc/hexane, 30:70). White solid: yield 92% (185.8 mg); mp 77–78 °C (lit.[24] 79–80 °C); R_f (50% EtOAc/hexane) 0.35; IR (KBr, cm^{-1}) 2231; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 8.0 Hz, 2H), 7.48 (d, J = 8.0 Hz, 2H), 3.55 (br, 2H), 3.20 (br, 2H), 1.26 (br, 3H), 1.11 (br, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 141.4, 132.4, 127.0, 118.1, 113.0, 43.2, 39.4, 14.2, 12.8; HRESI-MS (m/z) Calculated for $C_{12}H_{14}N_2O$ (M + Na) 225.1004 found (M + Na) 225.1003.

Methyl 4-Cyanobenzoate (2u). Prepared as described in the general experimental procedure. Purified on a silica gel column (EtOAc/hexane, 10:90). White solid: yield 94% (151.3 mg); mp 67–68 °C (lit.[25] 67–69 °C); R_f (15% EtOAc/hexane) 0.4; IR (KBr, cm^{-1}) 2231; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 8.4 Hz, 2H), 7.75 (d, J = 8.4 Hz, 2H), 3.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 133.8, 132.2, 130.0, 117.9, 116.3, 52.7; HRESI-MS (m/z) Calculated for $C_9H_7NO_2$ (M + H) 162.0555, found (M + H) 162.0552.

4-Hydroxy-3-nitrobenzonitrile (2v). Prepared as described in the general experimental procedure. Yellow solid: yield 94% (154.1 mg); mp 141–143 °C (lit.[26] 142–145 °C); R_f (15% EtOAc/hexane) 0.55; IR (KBr, cm^{-1}) 2228; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.90 (br, 1H), 8.48 (s, 1H), 7.83 (d, J = 8.8 Hz, 1H), 7.30 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ157.8, 139.5, 133.5, 130.1, 121.7, 116.6, 104.5; MS (m/z) 164.

4-Hydroxy-(1,1-biphenyl)-3-carbonitrile (2w). Prepared as described in the general experimental procedure. Solid: yield 51% (99.4 mg); mp 193–194 °C (lit.[27] 195 °C); R_f (15% EtOAc/hexane) 0.6; IR (KBr, cm^{-1}) 2225; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (s, 1H), 7.91 (s, 1H), 7.82 (d, 1H), 7.70 (d, 1H), 7.61 (d, 2H), 7.50 (t, 2H), 7.41 (t, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8, 146.4, 140.3, 137.7, 130.0, 128.9, 127.5, 127.4, 122.0, 120.0, 109.9; HRESI-MS (m/z) Calculated for $C_{13}H_9NO$ (M + H) 196.0762, found (M + H) 196.0760.

4-Ethanoylbenzonitrile (2x). Prepared as described in the general experimental procedure. White solid: yield 98% (142.1 mg); mp 56–57 °C (lit.[9a] 56–58 °C); R_f (15% EtOAc/hexane) 0.5; IR (KBr, cm^{-1}) 2227; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 8.4 Hz, 2H), 7.78 (d, J = 8.4 Hz, 2H), 2.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.5, 139.9, 132.5, 128.7, 117.9, 116.4, 26.7; MS (m/z) 145.

4-Cyanobenzoic Acid (2y). Prepared as described in the general experimental procedure. Yellow solid: yield 99% (145.5 mg); mp 208–209 °C (lit.[28] 209–211 °C); R_f (25% EtOAc/hexane) 0.1; IR (KBr, cm^{-1}) 2231; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.51 (br, 1H), 8.07 (d, J = 8.0 Hz, 2H), 7.97 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 135.3, 133.1, 130.3, 118.6, 115.4; MS (m/z) 147.

(*E*)-3-Phenylprop-2-enenitrile (3a).[9a] Prepared as described in the general experimental procedure. Colorless liquid: yield 98% (126.4 mg); R_f (15% EtOAc/hexane) 0.7; IR (Neat, cm^{-1}) 2218; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45−7.37 (m, 6H), 5.88 (d, J = 16.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.5, 133.4, 131.2, 129.1, 127.3, 118.1, 96.2; HRESI-MS (m/z) Calculated for C_9H_7N (M + H) 130.0657, found (M + H) 130.0653.

(*E*)-3-(4-Methoxyphenyl)prop-2-enenitrile (3b). Prepared as described in the general experimental procedure. White solid: yield 98% (155.8 mg); mp 63−65 °C (lit.[29] 62−65 °C); R_f (25% EtOAc/hexane) 0.65; IR (KBr, cm^{-1}) 2213; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 8.0 Hz, 2H), 7.33 (d, J = 16.8 Hz, 1H), 6.91 (d, J = 8.8 Hz, 2H), 5.71 (d, J = 16.4 Hz, 1H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.0, 150.0, 129.0, 126.3, 118.7, 114.5, 93.3, 55.4; HRESI-MS (m/z) Calculated for $C_{10}H_9NO$ (M + Na) 182.0582, found (M + Na) 182.0585.

(*E*)-3-(4-Nitrophenyl)prop-2-enenitrile (3c). Prepared as described in the general experimental procedure.Yellowish solid: yield 99% (172.2 mg); mp 198−200 °C (lit.[30] 200−201 °C); R_f (25% EtOAc/hexane) 0.56; IR (KBr, cm^{-1}) 2217; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, J = 8.8 Hz, 2H), 7.64 (d, J = 8.8 Hz, 2H), 7.48 (d, J = 16.8 Hz, 1H), 6.07 (d, J = 16.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.0, 147.7, 139.1, 128.1, 124.3, 117.0, 101.0; MS (m/z) 174.

2-Bromocyclohex-1-enecarbonitrile (3d). Prepared as described in the general experimental procedure. Colorless liquid: yield 60% (111.6 mg); IR (Neat, cm^{-1}) 2211; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.62−2.59 (m, 2H), 2.35−2.32 (m, 2H), 1.79−1.69 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.3, 118.1, 113.7, 36.2, 29.5, 23.2, 20.7; HRESI-MS (m/z) Calculated for C_7H_8BrN (M + Na) 207.9738, found (M + Na) 207.9737.

Typical Procedure for Gram Scale Synthesis of 4-Nitrobenzonitrile (2a). Triflic acid (30 mmol, 2.63 mL) was added dropwise during 10 min (***Caution!*** *reaction is exothermic*) to a well-stirred solution of aldehyde (10 mmol, 1.51 g), sodium azide (975 mg, 15 mmol) in CH_3CN (10 mL), and the mixture was stirred at room temperature until the reaction was completed (monitored by TLC, ∼2 min.). After removal of the solvent under reduced pressure, the residue was extracted with EtOAc (3 × 30 mL), and the combined organic extract was washed with water, dried over anhydrous Na_2SO_4, and purified by silica gel column using EtOAc/hexane (10:90) to furnish colorless solid **2a** (1.40 g, 95%).

■ ASSOCIATED CONTENT

Supporting Information

Characterization data (including ^{1}H and ^{13}C NMR spectra) for all products. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*Telephone: +91-80-22932887. Fax: +91-80-23600529. E-mail: prabhu@orgchem.iisc.ernet.in.

Notes

The authors declare no competing financial interest.

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(10) The reaction of 4-nitrobenzaldehyde, NaN_3, and TfOH in MeOH produced the corresponding dimethyl acetal along with unreacted starting material.

(11) Solvent screening studies with solvents such as $CHCl_3$, CH_2Cl_2, THF, toluene, EtOAc, MeOH, or DMF are carried out for only for 2 min, and the reactions were worked up. This is due to the reason that the reaction of 4-nitrobenzaldehyde, NaN_3, and TfOH in CH_3CN was complete almost instantaneously.

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(13) In the control experiments, it was observed that the reaction of triflic acid with aldehyde **1a** in CH_3CN is almost instantaneous (1 min) to furnish the product **2a** in quantitative yield. However, the same reaction of **1a** with other acids including concentrated H_2SO_4 in CH_3CN did not furnish the nitrile **2a** (see entries 2−7, Table 1). Therefore, we believe that acidity of acids used in this reaction plays a major role. Hence, triflic acid, which is a stronger acid than all other acids (pK_a is ∼ −15), works well for this reaction to form only the nitrile.

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