

# Succinic acid: a novel and efficient organo-catalyst for synthesis of $\alpha$ -amino nitriles under solvent free condition

Ramesh S. Ghogare  <sup>1\*</sup>

Department of Chemistry, B. N. N. College Bhiwandi, Dist-Thane, Maharashtra, India-421305

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**Abstract:** A simple, efficient and eco-friendly general protocol has been developed for the synthesis of three-component reaction methodology of Strecker's  $\alpha$ -amino nitriles by using various aldehyde or ketone, amines and trimethylsilyl cyanide (TMS-CN). In this methodology, succinic acid is used as a novel and efficient organo-catalyst in catalytic amount. This method was carried out under solvent free condition at room temperature for preparation of variety of  $\alpha$ -amino nitriles derivatives in excellent yields. The present method provides significant advantages of organo-catalyst such as inexpensive, highly stable, environmentally benign and commercially available as well as solvent free reaction conditions and high conversions of the products with excellent yield.

**Keywords:** Strecker reaction;  $\alpha$ -amino nitriles ; TMS-CN; succinic acid; organo-catalyst; solvent-free. ©2020 ACG Publication. All right reserved.

## 1. Introduction

In the recent years, an organocatalysis has been gained more attraction worldwide in the research of advanced organic chemistry because of their important characteristics including metal-free atmosphere, operational ease, reduced-cost and relatively less harmfulness<sup>1-6</sup>. It has been different mode of catalysis such as Brønsted acid-base catalysis, Lewis acid-base catalysis, Nucleophilic catalysis and Redox catalysis. An organo-catalyst is a simple organic molecule which is help to chemical transformation by activation of chemical reagents through various manners with increasing the mildness of the reaction conditions. One of these Brønsted acid catalysts, succinic acid has been used in the building block<sup>7</sup> for production of industrial chemicals<sup>8</sup>, plasticizers<sup>9</sup>, polyesters<sup>10</sup>, solvents<sup>11</sup> and biopolymers<sup>12</sup>. In the past years, for the efficient and practical chemical reaction condition, some methodologies have been reported by using succinic acid as catalysts in synthesis of  $\alpha$ -amino phosphonates<sup>13-14</sup> and Dihydropyridines<sup>15</sup>. Recently, we also reported succinic acid as catalyst for the synthesis of 3,4-disubstituted isoxazol-5(4*H*)-ones<sup>16</sup>. Herein, we described applicability of succinic acid as a readily available, efficient acidic organo-catalyst for the synthesis of  $\alpha$ -amino nitriles.

The Strecker reaction<sup>17-19</sup> is the first multi-component reaction (MCR) reported for the synthesis of  $\alpha$ -amino nitriles through the condensation of three-component of amine, cyanide and aldehyde in 1850.  $\alpha$ -amino nitriles are the key important bi-functional intermediate in the synthesis of versatile precursors of  $\alpha$ -amine acids<sup>20-21</sup>, biologically active molecules<sup>22-26</sup> and chiral building blocks<sup>27-30</sup>. In the view of the emerging importance of  $\alpha$ -amino nitriles, many of the researchers led to the development of efficient protocols using various catalysts, reagents and conditions. Recently, numerous methods have been developed for the synthesis of Strecker's  $\alpha$ -aminonitriles by using various catalysts such as Organo-catalysts<sup>31-38</sup>, Heterogeneous Brønsted acids<sup>39-45</sup>, Heterogeneous Lewis acids<sup>46-52</sup>, Homogeneous

\* E-Mail: [rsghogare05@gmail.com](mailto:rsghogare05@gmail.com)

Lewis acids<sup>53-59</sup>, Metals or Metal based complexes<sup>60-62</sup>, Ionic liquids<sup>63-67</sup> as well as Polymeric Materials<sup>68-69</sup>. In similar manner, different Solvent systems<sup>70-73</sup> and Cyanide sources<sup>74-78</sup> are also reported in the literature. Many of the reported methods involve one or two limitations such as, use of expensive reagents, harsh reaction conditions, extended reaction times, tedious workup procedures and low yields. In some cases, the catalysts are decomposed or deactivated by amines. Therefore, there is scope to develop efficient, milder conditions and environmental benign green chemical processes are major challenges for researcher in organic synthesis. As part of our ongoing research, to develop a novel methodology using alternative protocols<sup>79-80</sup> and by considering the importance  $\alpha$ -amino nitriles, herein, we report, a simple and efficient synthesis of  $\alpha$ -amino nitriles by using succinic acid as an organo-catalyst under solvent free condition. Succinic acid is mild, inexpensive, highly stable, environmentally benign and commercially available compound. In order to minimize toxicity of cyanide reagent, in this method TMS-CN is used as cyanide source for nucleophilic addition to the imines.

## 2. Experimental

### 2.1. Chemical Material and Apparatus

Reagents and solvents were purchased from commercial sources and used without further purification. <sup>1</sup>H NMR spectra were recorded on Gemini-300 spectrometer in CDCl<sub>3</sub> using TMS as an internal standard and IR spectra were recorded on a Bruker FT-IR spectrophotometer using neat or KBr disk. Mass spectra were recorded on a Finnigan MAT 1020 mass spectrometer operating at 70 eV. Melting points were determined with Buchi R-535 apparatus are uncorrected.

### 2.2. General Procedure

A mixture of aromatic aldehyde or ketone (1 mmol), amines (1 mmol) and TMS-CN (1.2 mmol) was stirred in presence of succinic acid (15 % mol) as catalyst under solvent free condition at room temperature. After completion of reaction monitored by thin layer chromatography, 10 ml water was added to the mixture and the product was extracted with ethyl acetate (2×10 ml). The combined ethyl acetate extract was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub> and the crude product was purified concentrated under reduced pressure by column chromatography using silica gel (60-120 mesh) by eluting with ethyl acetate-hexane mixture (2:8). All the pure products were confirmed by their spectroscopy data.

### 2.3. Spectral Data of Synthesized Compounds

*2-phenyl-2-(phenylamino)acetonitrile (4a)*: White solid; m.p. 78-80 °C (<sup>Lit</sup>[38] 81-83 °C); IR (KBr)  $\bar{\nu}$ = 3360, 3032, 2968, 2257, 1585, 1476, 1291, 1176, cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$ = 3.98 (d, 1H, *J* = 8.4 Hz, NH), 5.50 (d, 1H, *J* = 8.4 Hz, CH-CN), 6.81 (d, 2H, *J* = 8.2 Hz, ArH), 6.93 (t, 1H, *J* = 7.5 Hz, ArH), 7.26 (t, 2H, *J* = 7.5 Hz, ArH), 7.44 -7.56 (m, 3H, ArH), 7.78 -7.86 (m, 2H, ArH) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$ : 50.31, 114.6, 118.5, 120.5, 127.3, 128.7, 129.2, 133.7, 144.2 ppm. ESIMS: *m/z*: 209 (M<sup>+</sup>).

*2-((4-Nitrophenyl)amino)-2-phenylacetonitrile (4b)*: White solid; m.p. 125-127 °C (<sup>Lit</sup>[70] 127-129 °C); IR (KBr)  $\bar{\nu}$ = 3330, 2995, 2246, 1535, 1423, 1364, 1270, 1156 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$ = 4.76 (d, 1H, *J* = 7.1 Hz, -NH), 5.51 (d, 1H, *J* = 7.3 Hz, CH-CN), 6.77 (d, 2H, *J* = 9.2 Hz, ArH), 7.44 - 7.56 (m, 5H, ArH), 8.12 (d, 2H, *J* = 7.2 Hz, ArH) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$ = 48.4, 116.3, 116.6, 127.8, 128.9, 129.5, 133.3, 136.3, 151.6 ppm. ESIMS: *m/z*: 254 (M<sup>+</sup>).

*2-((4-fluorophenyl)amino)-2-phenylacetonitrile (4c)*: Yellow solid; m.p. 88-90 °C (<sup>Lit</sup>[70] 88-90 °C); IR (KBr)  $\bar{\nu}$ = 3348, 3064, 2242, 1579, 1466, 1293, 1196 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$ = 3.96 (brs, 1H, *J* = 5.6 Hz, -NH), 5.36 (d, 1H, *J* = 5.6 Hz, -CH-CN), 6.69-6.77 (m, 2H, ArH), 6.96 (t, 2H, *J* = 8.4 Hz, ArH), 7.42-7.49 (m, 3H, ArH), 7.54 -7.62 (m, 2H, ArH) ppm; <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$ : 50.0, 116.7, 120.3, 120.6, 127.0, 127.5, 133.2, 143.4, 151.3 ppm. ESIMS: *m/z*: 227 (M<sup>+</sup>).

2-((4-methoxyphenyl)amino)-2-phenylacetonitrile (**4d**): White solid; m.p. 74-76 °C (Lit<sup>[70]</sup> 75-77 °C); IR (KBr)  $\bar{\nu}$ = 3362, 2946, 2236, 1585, 1488, 1435, 1274, 1238,  $\text{cm}^{-1}$ . <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$ = 3.75 (s, 3H, -OCH<sub>3</sub>), 3.98 (d, 1H,  $J$  = 5.6 Hz, -NH), 5.34 (s, 1H, -CH-CN), 6.76 (d, 2H,  $J$  = 9.0 Hz, ArH), 6.85 (d, 2H,  $J$  = 9.0 Hz, ArH), 7.42-7.48 (m, 3H, ArH), 7.60 (dd, 2H,  $J_1$  = 5.9 Hz,  $J_2$  = 1.6 Hz, ArH) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$ : 48.4, 51.7, 114.9, 116.2, 127.4, 128.3, 134.0, 138.5, 150.1 ppm. ESIMS:  $m/z$ : 238 (M<sup>+</sup>).

2-morpholino-2-phenylacetonitrile (**4e**): White solid; m.p. 68-70 °C (Lit<sup>[70]</sup> 66-68 °C), IR (KBr)  $\bar{\nu}$ = 3015, 2949, 2848, 2239, 1601, 1528, 1435, 1274  $\text{cm}^{-1}$ . <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$ = 2.54-2.62 (m, 4H, 2-CH<sub>2</sub>), 3.68-3.78 (m, 4H, 2-CH<sub>2</sub>), 4.82 (s, 1H, -CH-CN), 7.36-7.44 (m, 3H, ArH), 7.54 (d, 2H,  $J$  = 7.3 Hz, ArH) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$ : 48.8, 62.5, 66.0, 116.0, 127.2, 127.9, 128.5, 130.6 ppm. ESIMS:  $m/z$ : 203 (M<sup>+</sup>).

(4-Methoxyphenyl)-2-(phenylamino)acetonitrile (**4f**): White solid; m.p. 94-96 °C (Lit<sup>[53]</sup> 95-96 °C), IR (KBr):  $\bar{\nu}$ = 3375, 3023, 2949, 2235, 1580, 1510, 1462, 1300,  $\text{cm}^{-1}$ ; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 3.76 (s, 3H, -OCH<sub>3</sub>), 3.96 (s, 1H, -NH), 5.35 (s, 1H, -CH-CN), 6.72 (d, 2H,  $J$ = 8.0 Hz, ArH), 6.88-6.98 (m, 3H, ArH), 7.18 (d, 2H,  $J$  = 8.0 Hz, ArH), 7.60 (d, 2H,  $J$  = 8.0 Hz, ArH), ppm; <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$ = 49.1, 52.0, 113.6, 115.3, 116.6, 120.6, 127.8, 128.6, 129.1, 144.8, 159.1 ppm. ESIMS:  $m/z$ : 239 (M<sup>+</sup>).

4-(cyano(phenylamino)methyl)benzonitrile (**4g**): Pale yellow solid; m.p. 120-122 °C (Lit<sup>[53]</sup> 116-118 °C), IR (KBr): 3370, 2868, 2245, 1610, 1530, 1450, 1265  $\text{cm}^{-1}$ . <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 4.70 (d, 1H,  $J$  = 7.5 Hz, -NH), 5.50 (d, 1H,  $J$  = 7.6 Hz, CH-CN), 6.80 (d, 2H,  $J$  = 7.8 Hz, ArH), 6.96 (t, 1H,  $J$  = 7.4 Hz, ArH), 7.38 (t, 2H,  $J$  = 7.6 Hz, ArH), 7.72 (d, 2H,  $J$  = 7.4 Hz, ArH), 7.76 (d, 2H,  $J$  = 7.4 Hz, ArH) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 48.6, 111.2, 111.6, 114.6, 118.5, 120.5, 127.5, 128.7, 129.3, 134.9, 143.9 ppm; ESIMS:  $m/z$ : 234 (M<sup>+</sup>)

3-phenyl-2-(phenylamino)propanenitrile (**4h**): Pale yellow solid; m.p. 108-110 °C, IR (KBr):  $\bar{\nu}$ = 3324, 3018, 2924, 2842, 2728, 2228, 1676, 1567, 1462, 1340, 1274  $\text{cm}^{-1}$ . <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$ = 3.10-3.30 (m, 2H, Ar-CH<sub>2</sub>), 4.36 (t, 1H,  $J$ = 6.3 Hz, -CH-CN), 6.76-6.84 (m, 3H, ArH), 7.30-7.42 (m, 5H, ArH), 7.48-7.56 (m, 2H, ArH) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz):  $\delta$  = 36.8, 50.3, 114.0, 116.3, 120.4, 126.9, 127.4, 128.6, 129.5, 132.7, 144.6 ppm. ESIMS:  $m/z$ : 245 (M<sup>+23</sup>).

2-(4-hydroxyphenylamino)-3-phenylpropanenitrile (**4i**): Pale yellow solid; m.p.. 133-135 °C (Lit<sup>[70]</sup> 136-138 °C), IR (KBr):  $\bar{\nu}$ = 3292, 3062, 2924, 2853, 2797, 2238, 1517, 1450, 1378, 1240  $\text{cm}^{-1}$ . <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$ = 3.12-3.30 (m, 2H, Ar-CH<sub>2</sub>), 4.38 (t, 1H,  $J$ = 6.3 Hz, -CH-CN), 4.74 (brs, 1H, -OH), 6.63 (d, 2H,  $J$  = 8.6 Hz, ArH), 6.75 (d, 2H,  $J$  = 8.6 Hz, ArH), 7.31-7.44 (m, 5H, ArH) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz):  $\delta$ = 39.0, 48.4, 116.3, 116.6, 127.8, 128.9, 129.5, 134.2, 138.3, 149.8 ppm. ESIMS:  $m/z$ : 239 (M<sup>+</sup>).

2-(furan-2-yl)-2-(phenylamino)acetonitrile (**4j**): Brown solid; m.p. 70-72 °C (Lit<sup>[44]</sup> 67-69 °C); IR (KBr):  $\bar{\nu}$ = 3365, 3040, 2945, 2254, 1590, 1542, 1475, 1325  $\text{cm}^{-1}$ . <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$ = 4.04 (d, 1H,  $J$  = 5.6 Hz), 5.48 (s, 1H, -CH-CN), 6.42 (d, 1H,  $J$  = 3.8 Hz, ArH), 6.58 (t, 1H,  $J$  = 4.7 Hz, ArH), 6.74 (d, 2H,  $J$  = 7.8 Hz, ArH), 6.90 (t, 1H,  $J$  = 7.8 Hz, ArH), 7.36 (t, 2H,  $J$  = 7.8 Hz, ArH), 7.52 (d, 1H,  $J$  = 4.7 Hz, ArH) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$ = 47.8, 111.1, 112.0, 115.9, 121.5, 129.5, 134.2, 136.9, 145.8, ppm. ESIMS:  $m/z$ : 199 (M<sup>+</sup>).

2-(9H-fluoren-2-yl)-2-(phenylamino)acetonitrile (**4k**): Gray solid; m.p.. 152-154 °C (Lit<sup>[70]</sup> 152-154 °C); IR (KBr):  $\bar{\nu}$ = 3384, 2924, 2854, 2228, 1510, 1459, 1221  $\text{cm}^{-1}$ . <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$ = 3.94 (s, 2H, -CH<sub>2</sub>), 5.49 (d, 1H,  $J$  = 8.2 Hz, -CH-CN), 6.81 (d, 2H,  $J$  = 7.6 Hz, ArH), 6.85-6.95 (m, 1H, ArH), 7.24-7.38 (m, 4H, ArH), 7.59 (t, 2H,  $J$  = 8.5 Hz, ArH), 7.78-7.87 (m, 3H, ArH) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>,

75 MHz):  $\delta$ = 36.8, 50.3, 114.0, 118.4, 120.2, 120.3, 120.4, 123.9, 125.1, 126.0, 126.9, 127.4, 129.5, 132.0, 140.5, 143.0, 143.4, 144.2, 144.6 ppm. ESIMS:  $m/z$ : 295 ( $M^+$ ).

*2-(9H-fluoren-2-yl)-2-(4-methoxyphenylamino)acetonitrile (4l)*: Brown solid; m.p.. 140-142 °C (<sup>lit</sup>[70] 144-146 °C); IR (KBr):  $\bar{\nu}$ = 3332, 2925, 2853, 2227, 1604, 1511, 1459, 1287, 1244  $cm^{-1}$ . <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$ = 3.78 (s, 3H, -OCH<sub>3</sub>), 3.94 (s, 2H, -CH<sub>2</sub>), 5.41 (d, 1H,  $J$  = 6.4 Hz, -CH-CN), 6.79 (d, 2H,  $J$  = 9.0 Hz, ArH), 6.86 (d, 1H,  $J$ =8.2 Hz, ArH), 7.31-7.43 (m, 3H, ArH), 7.58 (t, 2H,  $J$ =8.7 Hz, ArH), 7.82-7.87 (m, 2H, ArH) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz):  $\delta$ = 36.8, 51.7, 55.6, 114.9, 116.2, 120.2, 120.4, 122.1, 123.9, 124.5, 125.1, 126.0, 126.9, 127.4, 128.3, 132.3, 138.5, 140.6, 143.4, 144.2, 158.6 ppm. ESIMS:  $m/z$ : 327 ( $M^+$ ).

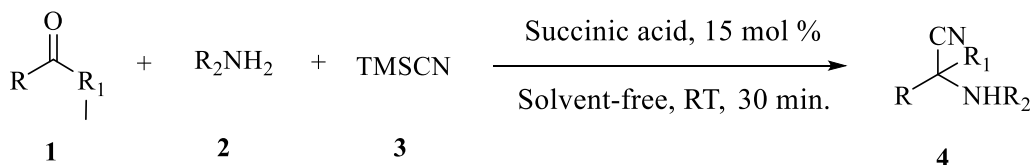
*2-(9H-fluoren-2-yl)-2-morpholinoacetonitrile (4m)*: White solid; m.p. 175-177 °C (<sup>lit</sup>[70] 176-178 °C); IR (KBr):  $\bar{\nu}$ = 2929, 2862, 2819, 2230, 1686, 1458, 1294  $cm^{-1}$ . <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$ = 2.56-2.70 (m, 4H, 2-CH<sub>2</sub>), 3.68-3.82 (m, 4H, 2-CH<sub>2</sub>), 3.93 (s, 2H, -CH<sub>2</sub>), 4.90 (s, 1H, -CH-CN), 7.30-7.47 (m, 2H, ArH), 7.50-7.64 (m, 2H, ArH), 7.70-7.76 (m, 1H, ArH), 7.78-7.88 (m, 2H, ArH) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz):  $\delta$ = 36.8, 49.9, 62.5, 66.6, 115.4, 119.9, 120.1, 124.6, 125.0, 126.7, 126.8, 127.2, 130.6, 140.6, 142.6, 143.4, 143.7 ppm. ESIMS:  $m/z$ : 291( $M^+$ ).

*2-phenyl-2-(phenylamino)propanenitrile (4n)*: Pale yellow solid; m.p. 138-140 °C (<sup>lit</sup>[57] 133-136 °C). IR (KBr):  $\bar{\nu}$ = 3357, 2985, 2867, 2236, 1671, 1468, 1254,  $cm^{-1}$ . <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$ = 1.72 (s, 3H, -CH<sub>3</sub>), 4.07 (s, 1H, -NH), 6.31 (d, 2H,  $J$  = 8.4 Hz), 6.56 (t, 1H,  $J$  = 8.2 Hz), 6.88 (t, 2H,  $J$  = 8.2 Hz, ArH), 7.12-7.21 (m, 3H, ArH), 7.45 (d, 2H,  $J$  = 7.4 Hz, ArH) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$ = 33.7, 57.5, 114.0, 120.2, 120.4, 125.1, 128.3, 129.1, 129.5, 139.5, 143.4 ppm. ESIMS:  $m/z$ : 222 ( $M^+$ )

*2-((4-methoxyphenyl) amino)-2-phenylpropanenitrile (4o)*: Pale yellow solid; m.p. 93-95 °C (<sup>lit</sup>[59] 88-90 °C). IR (KBr):  $\bar{\nu}$ = 3357, 2965, 2843, 2236, 1624, 1438, 1254  $cm^{-1}$ . <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$ = 2.40 (s, 3H, -CH<sub>3</sub>), 4.18 (s, 3H, -OCH<sub>3</sub>), 4.51 (s, 1H, -NH), 7.04 (d, 2H,  $J$  = 9.0 Hz, ArH), 7.17 (d, 2H,  $J$  = 9.2 Hz, ArH), 7.80-7.88 (m, 3H, ArH), 8.10 (d, 2H,  $J$  = 7.5 Hz, ArH) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$ = 31.4, 55.6, 58.7, 112.3, 117.7, 125.7, 127.8, 129.0, 137.5, 139.9, 152.5, 158.0 ppm. ESIMS:  $m/z$ : 252 ( $M^+$ )

### 3. Results and Discussion

According to our previous studies concerning the use of succinic acid as an efficient acid catalyst for synthesis of 3,4-disubstituted isoxazol-5(4*H*)-ones. Here, we used succinic acid as catalyst for synthesis of  $\alpha$ -aminonitriles. In this typical experiment, reaction occurs between aromatic aldehyde or ketone (**1**), amines (**2**) and TMS-CN (**3**) in the presence of succinic acid as an organo-catalyst at room temperature. The reaction was completed within 30 minutes and obtained the corresponding  $\alpha$ -amino nitriles (**4a**) derivative were in excellent yields as shown in the general Scheme 1.



$\text{R}$ = aryl or alkyl,  $\text{R}_1$ = H or alkyl,  $\text{R}_2$ = aryl or alkyl

**Scheme 1.** Synthesis of  $\alpha$ -amino nitriles catalyzed by succinic acid

To optimize the reaction conditions as well as catalyst, initially the reaction was carried out in the absence of catalyst under solvent free condition but desired product was not observed even extending the reaction time. So the use of catalyst is necessary for improvement of reaction. By considering the importance of catalyst, we chose mild, highly stable, less harmful and commercially cheaply available Succinic acid as catalyst.

**Table 1.** Optimization of catalyst

No	Succinic acid (mol %)	Time (min.)	Time (min.)
1	No catalyst	120	NR*
2	5	30	35
3	10	30	55
<b>4</b>	<b>15</b>	<b>30</b>	<b>90</b>
5	20	30	87

NR\* = No Reaction (Product not formed)

Initially, the role of the catalyst was monitored by using different mole ratio from 5-20% under solvent free condition. The yield of product gradually increases with increasing the amount of catalyst till 15% mole, but after increasing the amount of catalyst more than 15% mol, causes gradually decreases the yield of products. The observation shows that 15% mole equivalent of succinic acid is sufficient for the completion of reaction. All the results are summarized in Table 1.

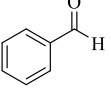
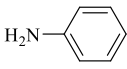
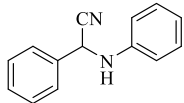
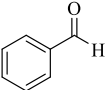
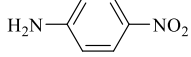
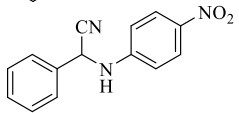
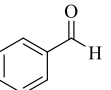
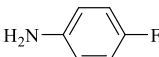
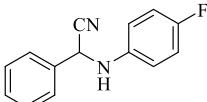
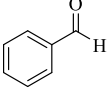
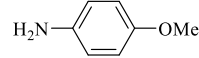
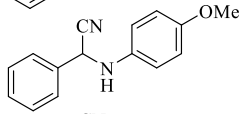
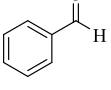
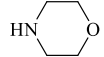
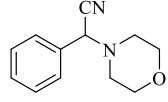
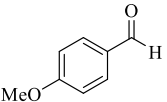
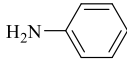
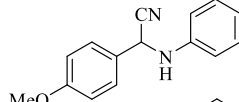
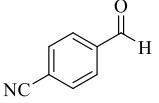
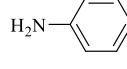
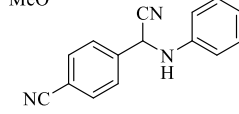
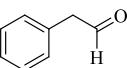
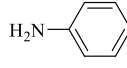
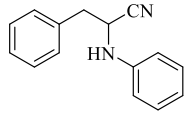
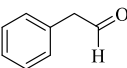
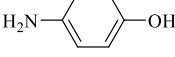
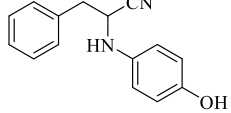
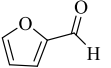
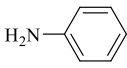
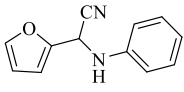
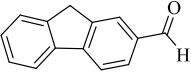
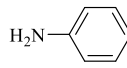
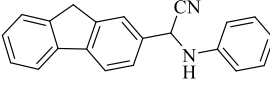
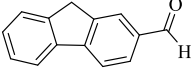
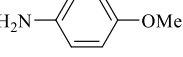
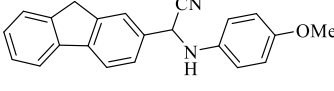
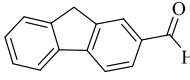
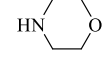
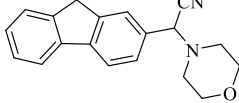
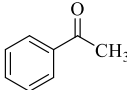
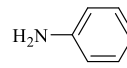
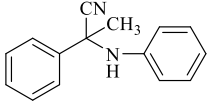
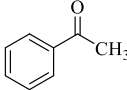
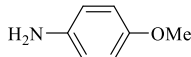
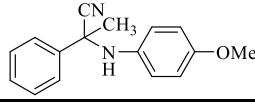
After optimization of catalyst, we concentrated on screening of solvent system. Initially, the reaction was carried out in water using 15% mol of catalyst and the corresponding  $\alpha$ -amino nitrile (**4a**) was obtained only in 45% yield. Due to this low yield, we moved to try other solvents systems such as tetrahydrofuran, dichloromethane, acetone, ethanol and yield of corresponding product **4a** obtained with 57, 62, 65 and 70 % respectively. In above all solvents, products yield were somewhat improved but failed to achieve the expected results which is obtained in solvent free condition. The observation shows that a solvent free condition is best reaction condition in terms of the completion of reaction and yield of products. The yield of the product may be increased under solvent free condition due to the greater interaction between the reactant molecules and catalyst. All the results are summarized in Table 2.

**Table 2.** Optimization of reaction solvent

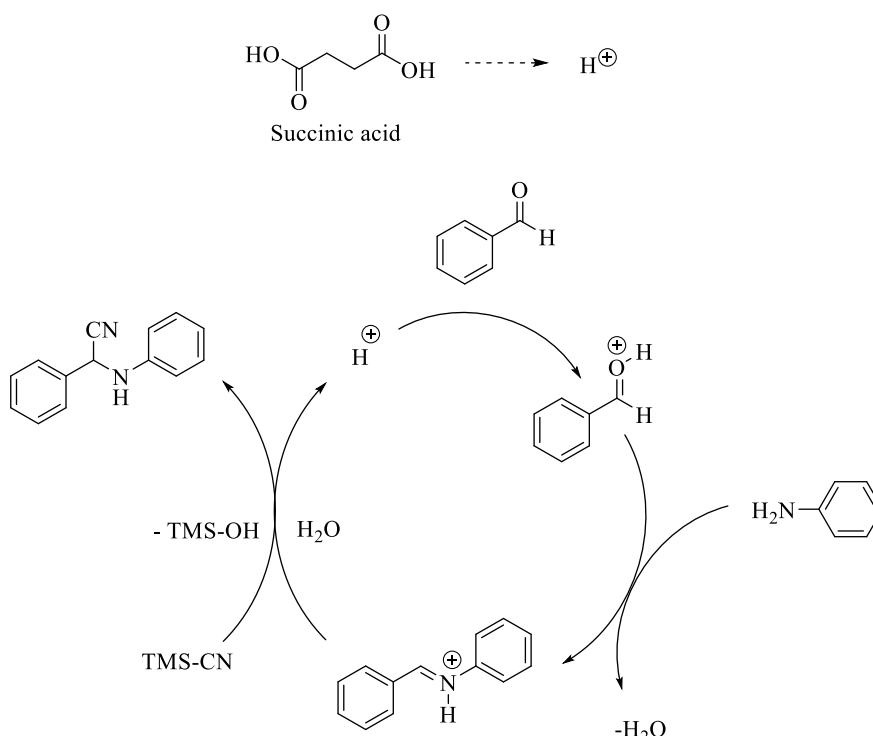
No	Solvent	Succinic acid (mol %)	Time (min)	Isolated Yields (%)
1	Solvent-free	15	30	90
2	Water	15	30	45
3	Tetrahydrofuran	15	30	57
4	Dichloromethane	15	30	62
5	Acetone	15	30	65
6	Ethanol	15	30	70

By encouraged with results obtained in above optimal reaction conditions, the reaction was performed using various aromatic aldehydes and ketones with variety of amines and TMS-CN for the synthesis of  $\alpha$ -amino nitriles (**4a-4o**) to demonstrate the applicability of the catalyst (Table 3). The feasibility of formation of products and its yields are depends on various electronic as well as steric factors presence on aldehydes or ketones and amines. The aromatic aldehyde having electron withdrawing group obtained in excellent yield while electron donating group gives somewhat decreased yield and in terms of aromatic amines, the results of products yield are vice versa. The reactivity of ketone compared to aldehyde decreases, due to presence of alkyl group, which creates the steric hindrance around carbonyl carbon and due to this steric hindrance; nucleophile does not reach easily at carbonyl carbon for the addition reaction.

**Table 3.** Synthesis of  $\alpha$ -aminonitriles in the presence of succinic acid under solvent-free condition

No	Aldehyde/ Ketone	Amines	Products	Yield (%) <sup>a</sup>
a				90
b				85
c				86
d				92
e				88
f				85
g				92
h				90
i				91
j				90
k				90
l				92
m				88
n				70
o				75

<sup>a</sup>Isolated yield



**Scheme 2.** Probable reaction mechanism

The product formation can be explained as shown in plausible reaction mechanism (Scheme-2). The acidic proton of succinic acid has activated the carbonyl carbon of aromatic aldehyde by making coordination with carbonyl oxygen, which leads to formation of imine with aromatic amines. Then the nucleophilic addition reaction occurs between active imines group and trimethylsilyl cyanide to form the desired product.

#### 4. Conclusion

In summary, we have demonstrated a simple, efficient and novel three-component methodology for the synthesis of Strecker's  $\alpha$ -amino nitriles by using various aldehyde or ketone, amines and TMS-CN. The present method offers significant advantages such as inexpensive catalyst, solvent free, mild reaction conditions, high conversions and excellent yield.

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#### Supporting Information

Supporting information accompanies this paper on <http://www.acgpubs.org/journal/organic-communications>

ORCID 

Ramesh S. Ghogare: [0000-0003-0810-9636](https://orcid.org/0000-0003-0810-9636)

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