Chapter 5

One Pot Facile Synthesis of Propynenitriles from 3-Chloropropenals
Chapter 5. One Pot Facile Synthesis of Propynenitriles from 3-Chloropropenals

5.1. Motivation for the current work

The chemistry of variously substituted acetylenes has felt a renaissance in the past decade not only due to their importance in biochemistry and material science, but also as building blocks as well as versatile intermediates for synthesis of a vast array of heterocyclic moieties of potential medicinal interest. The carbon-carbon triple bond of alkynes is one of the constitutional functional groups in organic chemistry exhibiting the fundamental reactions of synthetic utility. Furthermore, cyano group has always been envisaged as a fountainhead of functionalization in organic medicinal chemistry due to its facile transformation to functional groups of medicinal significance such as amines, amides, amidines, aldehydes, ketones, carboxylic acids esters etc. Combination of these two versatile functionalities, viz. alkyne and cyano, in alkynenitriles make these as much sought after intermediates of potential synthetic as well as medicinal importance. Alkynenitriles serve as essential structural units for synthesis of a variety of five or six membered carbocycles and heterocycles such as

![Diagram of general synthetic applications of alkynenitriles](image)

Figure 5.1. General synthetic applications of alkynenitriles.
cyclopentadienones, \(^2\) \(^3\) 1,2,3-triazoles, \(^4\) \(^5\) isoxazoles, \(^6\) iminopyrimidines, \(^7\) benzo[b]phospholes, \(^8\) benzopyranes, \(^9\) thiophenes, \(^10\) benzofurans, \(^10\) pyrroles, \(^11\) indoles, \(^12\) etc. (Figure 5.1).

In view of their importance as intermediates in organic synthesis, many methods for preparation of alkynenitriles have been documented in literature. Most of these methods involve the use of toxic reagents like cyanogen halides or other organo based cyanating agents, dehydrating agents, oxidizing agents etc. Further, the utility of these methods is limited by the formation of side products, difficult preparation of starting precursors and low yields. Fascinating profile of these starting units coupled with our ongoing interest in developing better methods for heterocyclic precursors, \(^13\) \(^14\) we envisioned to develop a simple and efficient one pot methodology for their preparation. Here, in this chapter, we report an efficient one pot procedure for the preparation of alkynenitriles (2) starting from readily available chloropropenals (1) (Scheme 5.1).

\[
\begin{align*}
&\text{Ar} \quad \text{Cl} \quad \text{CHO} \quad \text{Aq. NaOH} \quad \text{THF} \\
&\text{1} \quad \text{Ar} \equiv \equiv \text{CN} \quad \text{2}
\end{align*}
\]

**Scheme 5.1**

### 5.2. Results and discussion

Numerous methods have already been developed for the preparation of alkynenitriles. A thorough review of literature revealed that most of these methods may broadly be classified under two main strategies for the synthesis of alkynenitriles. The first strategy includes introduction of a cyano group to terminal alkynes which involves the conversion of alkynes to metallated acetylides using a base and then its treatment with a cyanating agent. In the second strategy, a functional group already present at alkyne is converted to nitrile by using suitable dehydrating or oxidizing agent. Besides these, some miscellaneous methods are also reported in literature for the preparation of alkynenitriles. All the available methods are discussed in the following section.

**A. Cyanation of terminal alkynes**

Introduction of cyano group to the terminal alkynes via carbon-carbon bond formation is the fundamental strategy that has been explored widely for the
preparation of alkynenitriles. The underlying mechanism of this approach involves the conversion of terminal alkyne to metal acetylide followed by its nucleophilic attack on either a cyanating agent or $^+$CN ion furnished by a cyanating agent. A large number of cyanating agents such as cyanogen bromide,$^{15}$ cyanogen iodide,$^{16}$ cuprous cyanide,$^{17}$ 1-cyanobenzotriazole,$^{18}$ phenylcyanate,$^{19}$ 1-cyanoimidazole,$^{20}$ and 2-pyridylcyanate$^{21}$ have been employed with the aim to improve yields and minimize the hazardous effects of their toxicity.

Compagnon and Grosjean$^{15}$ reported the synthesis of phenylpropynenitrile by cyanation of copper(I) phenylacetylenide with cyanogen bromide by refluxing in a solvent mixture of diethyl ether and acetonitrile. Limited substrate scope and formation of diphenylbutadiyne as side product are the major drawbacks of the method (Scheme 5.2).

![Scheme 5.2](image)

Luo et al.$^{17}$ reported the preparation of alkynenitriles by reaction of arylacetylenes with stoichiometric amount of cuprous cyanide in the presence of chlorotrimethylsilane and sodium iodide as the catalyst (Scheme 5.3).

![Scheme 5.3](image)

The first attempt to perform cyanation of terminal alkynes by using a metal reagent in catalytic amount was done by Okamoto et. al.$^{16}$ using cyanogen iodide (ICN) as the cyanation agent leading to formation of alkynylcyanides. The reaction involves the noncatalyzed formation of alkynyliodide followed by copper-catalyzed cyanation of iodide with the formation of copper(I)acetylide. Alkynes with primary, secondary and tertiary alkyl groups, aliphatic acetylenes bearing various functional groups such as ether, chloro, ester and alkene moieties as well as para-substituted aromatic acetylenes tolerated the reaction conditions and afforded the corresponding cyanides with these functional groups intact (Scheme 5.4).
Cyanation of arylacetylenes has been achieved by Hughes and Cava\textsuperscript{18} employing 1-cyanobenzotriazole as cyanating agent. The phenylacetylene was first converted to its anion by lithiation with LDA and then its cyanation resulting in the formation of phenylpropynenitrile in good yield (Scheme 5.5).

\[ \text{Ar} \equiv \text{H} \xrightarrow{1. \text{LDA}} \xrightarrow{2. \text{CN}} \text{Ar} \equiv \text{CN} \]

\textbf{Scheme 5.5}

Wu et al.\textsuperscript{20} have reported another example of cyanation by using 1-cyanoimidazole as cyanating agent, but it need to be prepared from reaction of cyanogen bromide with imidazole. The methodology involves the conversion of phenylacetylene into acetylenide ion followed by an addition-elimination reaction with 1-cyanoimidazole (Scheme 5.6).

\[ \text{Ar} \equiv \text{H} \xrightarrow{1. \text{n-BuLi/THF}} \xrightarrow{2. \text{CN}} \text{Ar} \equiv \text{CN} \]

\textbf{Scheme 5.6}

Phenylpropynenitrile was also prepared by treatment of lithiumacetylenide with phenylcyanate in ether solvent in good yield as reported by Murray and Zweifel.\textsuperscript{19} Again, the preparation of phenyl cyanate from cyanogen bromide limits the utility of this method (Scheme 5.7).

\[ \text{Ph} \equiv \text{Li} + \text{C}_{6} \text{H}_{5} \text{OCN} \xrightarrow{\text{n-pentane or ether}} \text{Ph} \equiv \text{CN} \]

\textbf{Scheme 5.7}
Koo and Lee\textsuperscript{21} reported the preparation of alkynenitriles using Grignard reagents of alkynes acting as nucleophile and 2-pyridyl cyanate as the cyanating agent (Scheme 5.8).

\[
\begin{align*}
\text{Ar} & \equiv \text{MgBr} + \text{EtO-C-OC-N} \rightarrow \text{Ar} \equiv \text{CN} \\
\text{Scheme 5.8}
\end{align*}
\]

**B. Transformation of substituted alkynes to alkynenitriles**

Other strategy for preparation of alkynenitriles involves the transformation of a functional group such as aldehyde, alcohol, amide, azide etc. already present at alkyne into nitrile using either dehydrating agents or oxidizing agents.

Alkynes substituted with primary alcohols have been transformed into alkynenitriles by treatment with ammonia in isopropyl alcohol and THF containing magnesium sulphate and manganese dioxide.\textsuperscript{22} The transformation involves conversion of alcohol to aldehyde and then to aldimine followed by \textit{in situ} oxidation leading to the formation of corresponding nitrile. Recently, similar transformation has also been achieved by using 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO), iodosobenzene diacetate and ammonium nitrate by Vatele\textsuperscript{23} (Scheme 5.9).

\[
\begin{align*}
\text{Ar} & \equiv \text{CH}_2\text{OH} \rightarrow \text{NH}_3 \cdot \text{IPA, MgSO}_4, \text{MnO}_2
\end{align*}
\]

\[
\begin{align*}
\text{Ref. 22}
\end{align*}
\]

\[
\begin{align*}
\text{Ar} & \equiv \text{CN} \\
\text{TEMPO, PhI(OAc)}_2, \text{NH}_4\text{OAc}
\end{align*}
\]

\[
\begin{align*}
\text{Ref. 23}
\end{align*}
\]

\[
\begin{align*}
\text{Scheme 5.9}
\end{align*}
\]

There is a recent report on conversion of aldehydes into nitriles by reaction of aldehydes with hydroxylamine hydrochloride in presence of propylphosphonic anhydride (T\textsubscript{3}P) which is nontoxic coupling agent used for the first time here for dehydration purpose (Scheme 5.10).\textsuperscript{24}

\[
\begin{align*}
\text{Ph} & \equiv \text{CHO} \rightarrow \text{NH}_2\text{OH-HCl (1.1 equiv)} \rightarrow \text{Ph} \equiv \text{CN}
\end{align*}
\]

\[
\begin{align*}
\text{T\textsubscript{3}P (1.1 equiv)}
\end{align*}
\]

\[
\begin{align*}
\text{Et}_3\text{N, solvent}
\end{align*}
\]

\[
\begin{align*}
\text{Ph} \equiv \text{CN} + \text{Ph-O-N}
\end{align*}
\]

\[
\begin{align*}
\text{Scheme 5.10}
\end{align*}
\]
Alkynylnitriles have also been prepared by one pot conversion from alkynyl carboxylic acids using ethylpolyphosphate (PPE) (Scheme 5.11).25

\[
\text{Ph-COOH + NH}_3 \xrightarrow{\text{PPE/CHCl}_3 - \text{H}_2\text{O}} \text{Ph-CCONH}_2 \xrightarrow{\text{PPE} - \text{H}_2\text{O}} \text{Ph-CN}
\]

Scheme 5.11

Treatment of carboxamides under Swern oxidation conditions and Et\textsubscript{3}N, as dehydrating agent also give desired nitriles (Scheme 5.12).26,27

\[
\text{Ph-CCONH}_2 \xrightarrow{(\text{COCl})_2-\text{DMSO}} \text{Et}_3\text{N} \xrightarrow{\text{Ph-CN}} \text{Ph-CN}
\]

Scheme 5.12

Recently Wang et. al 28 have reported oxidative transformation of aryl propargyl azides to aryl propiolonitriles by using a copper(I) catalyst. Aryl propiolonitride derivatives were obtained in moderate to good yields by this oxidative Schmidt rearrangement (Scheme 5.13).

\[
\text{Ar-CH}_2\text{N}_3 \xrightarrow{\text{Cu(I)/O}} \text{-N}_2 \xrightarrow{\text{Ar-CN}} \text{Ar-CN}
\]

Scheme 5.13

C. Miscellaneous methods for alkynylnitriles

D. Armesto et.al. 29 have reported formation of 3-phenylpropynitrile as one of the products of photolysis of 4\textit{H}-pyrans (Scheme 5.14).

\[
\text{Ph-CN} \xrightarrow{\text{H}_2\text{NO}_2, \text{AcOH}} \text{Ph-CN} + \text{Ph-CN} + \text{Ph-CN}
\]

Scheme 5.14

5-Aminoisoaxozoles bearing at least one electron-withdrawing group react with sodium nitrite in aqueous acetic acid solution to give substituted acetylenes (Scheme 5.15).30

\[
\text{Ph-CN} \xrightarrow{\text{NaNO}_2, \text{AcOH}} \text{Ph-CN}
\]

Scheme 5.15
Interesting results were obtained when Ayi and Guedj\textsuperscript{31} were attempting the synthesis of 2-amino-3-fluoronitriles from 2-hydroxy-3-fluoronitriles by treating with dry ammonia in methanol in the presence of anhydrous magnesium sulphate. Surprisingly, cyanoalkyne was obtained instead of the expected product when they took 3-phenyl substituted reactant (Scheme 5.16).

\begin{equation}
\begin{aligned}
\text{R}_1\text{F} \text{OH} &\quad \text{MeOH}/\text{NH}_3 \quad \text{MgSO}_4, \text{ r.t.} \quad \text{PhCN} \\
\text{R}_1\text{CN} &\quad \text{R}_1, \text{R}_2 \quad \text{alkyl} \\
\text{R}_1\text{NH}_2 &\quad \text{alkyl} \\
\text{PhCN} &\quad \text{phenyl} \\
\text{H} &\quad \text{H}
\end{aligned}
\end{equation}

Scheme 5.16

Oxo-ylids on microwave irradiation give the corresponding acetylenes in high yield through the intermediate formation of oxaphosphete (Scheme 5.17).\textsuperscript{32}

\begin{equation}
\begin{aligned}
\text{Ph}_3\text{P} &\quad \text{CCl}_3\text{CN} \quad \text{MW, 5-7 min.} \quad \text{Ph}_3\text{PO} \\
\text{Ph}_3\text{P} &\quad \text{Ph} \quad \text{Ph} \quad \text{Ph}
\end{aligned}
\end{equation}

Scheme 5.17

Kim et. al\textsuperscript{33} have reported an efficient one pot procedure for preparation of conjugated alkynenitriles by reacting aldehydes with Ph\textsubscript{3}P and CCl\textsubscript{3}CN (Scheme 5.18).

\begin{equation}
\begin{aligned}
\text{Ph}_3\text{P} &\quad \text{CCl}_3\text{CN} \quad \text{BuLi (1 equiv)} \quad \text{BuLi (1.5 equiv)} \quad \text{R} \quad \text{CN} \\
\text{RCHO} &\quad \text{RCHO} \quad -78 \degree \text{C, 1 h}
\end{aligned}
\end{equation}

\text{R} = \text{alkyl, aryl and heteroaryl}

Scheme 5.18

In the previous chapter, we reported an eco-friendly, inexpensive and elegant methodology for the synthesis of 3-chloropropenenitriles from 3-chloropropenals (Section 4.1.2). We developed this methodology based on our initial isolation and characterization of 3-phenyl-3-chloropropenenitrile (3a) from the gummy mass of a mixture of products obtained by the reaction of 3-chloro-3-phenylpropenal (1a) with molecular iodine (1eq.) and aqueous ammonia in THF as solvent (Scheme 5.19). Though, we could successfully develop the methodology for exclusive formation of 3-
phenyl-3-chloropropeninitrile (3a), resolving the whole mixture to its pure components was still a challenge to us. Therefore, in our next attempt of analyzing the rest of the unidentified mass, we focused on investigating the step responsible for the side reactions and thus leading to the formation of a mixture of products.

If we carefully examine the structure of chloropropenals, there are three reactive centres i.e a formyl group, a hydrogen atom at $\alpha$-position and a chlorine atom at $\beta$-position to the formyl group. Since the conversion of aldehyde group to nitrile by treatment with molecular iodine and aqueous ammonia in THF as solvent is well documented in literature, therefore, the possibility of side reactions can best be expected through the involvement of $\alpha$-hydrogen or $\beta$-chlorine in the reaction either individually or simultaneously. Further, as we were precisely focused on examining the mechanism of reaction of 3-chloropropenals with molecular iodine and aqueous ammonia in THF as solvent leading to the formation of a mixture of products, it was intriguing to know the fate of 3-chloropropenals either with molecular iodine under neutral conditions or with molecular iodine under ammonia free (to avoid the formation of aldimine and hence the nitrile) basic conditions. With this in mind, first of all, we attempted the reaction of 3-phenyl-3-chloropropenal (1a) with molecular iodine (1 eq.) at room temperature using THF as solvent (Scheme 5.20). No reaction was observed even after stirring the reaction mixture for about 10 hours and 1a could be recovered as unreacted reactant.

Then we attempted the reaction of 3-phenyl-3-chloropropenal (1a) with molecular iodine (1 eq.) under ammonia free basic conditions employing various
organic and inorganic bases in THF as solvent (Scheme 5.21). None of the bases reacted with 1a even after stirring the reaction mixture for 10 hours and again the reactant could be recovered.

![Scheme 5.21](image)

This led us to conclude that 3-chloropropenal is first converted to 3-chloropropenenitrile in presence of I₂ and NH₃ followed by some side reactions under basic conditions leading to the formation of mixture of products (Scheme 5.22).

![Scheme 5.22](image)

Therefore, in our next experiment, we envisaged to react 3-chloropropenenitrile with molecular iodine alone as well as with molecular iodine under basic conditions using different bases including aqueous ammonia. The results are presented in Table 5.1. Treatment of 3a with molecular iodine (1 eq.) and aqueous ammonia in THF as solvent led to the formation of a mixture of products (Entry 1) as visualized on TLC. Surprisingly, a single product was seen on TLC plate when 3a was treated with molecular iodine and aqueous sodium hydroxide (1 eq.) at room temperature for 3h leading to complete consumption of reactant 3a as evident from TLC of reaction mixture (Entry 2). The new product formed appeared as a single spot at an Rₜ value just above the reactant and was isolated and identified as 3-phenylpropynenitrile 2a on the basis of its spectral analysis. 3-Phenylpropynenitrile 2a was also formed as a single product when 3a was treated with molecular iodine and aqueous sodium bicarbonate but the reaction was incomplete after 3 hours (Entry 3). No reaction occurred when TEA, pyridine or piperidine were used alongwith molecular iodine (Entry 4, 5 and 6). Next we investigated the role of iodine in the reaction and carried out the reaction of 3a with aqueous ammonia without using iodine and the same
mixture of products was obtained (Entry 7) but using aq. NaOH solution alone again led to the formation of 2a exclusively (Entry 8). Next we attempted to optimize the reaction time and found that reaction takes just 15 minutes for complete conversion of 3-chloropropenenitriles to propynenitrile. These results validated our assumption that the reaction of 3-chloro-3-phenylpropenal (1a) with I₂ and NH₃ first leads to the formation of 3-phenyl-3-chloropropenenitrile (3a) which further reacts under the reaction conditions to give a mixture of products including 3-phenylpropynenitrile (2a). Thus, in this study, we successfully identified another component of the mixture of products obtained on treatment of 3-phenyl-3-chloropropenal with molecular iodine and aqueous ammonia in THF and also developed the methodology for the preparation of propynenitriles. We are still not sure about the other products in the reaction of 3-chloro-3-phenylpropenal (1a) and 3-phenylpropynenitrile (2a) as more than two spots are visible on TLC under original reaction conditions of molecular iodine, aqueous ammonia and THF.

Table 5.1. Study of reaction 3-chloro-3-phenylpropenenitrile (3a) with molecular iodine and/or different bases in THF as solvent at room temperature.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Conditions</th>
<th>Product(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>I₂ (1 eq.) + aq. ammonia</td>
<td>mixture</td>
</tr>
<tr>
<td>2.</td>
<td>I₂ (1 eq.) + aq. NaOH (1 eq.)</td>
<td>2a</td>
</tr>
<tr>
<td>3.</td>
<td>I₂ (1 eq.) + aq. NaHCO₃ (1 eq.)</td>
<td>2a but incomplete reaction</td>
</tr>
<tr>
<td>4.</td>
<td>I₂ (1 eq.) + TEA (1 eq.)</td>
<td>No reaction</td>
</tr>
<tr>
<td>5.</td>
<td>I₂ (1 eq.) + pyridine (1 eq.)</td>
<td>No reaction</td>
</tr>
<tr>
<td>6.</td>
<td>I₂ (1 eq.) + piperidine (1 eq.)</td>
<td>No reaction</td>
</tr>
<tr>
<td>7.</td>
<td>Aq. ammonia</td>
<td>mixture</td>
</tr>
<tr>
<td>8.</td>
<td>Aq. NaOH (1 eq.)</td>
<td>2a</td>
</tr>
<tr>
<td>9.</td>
<td>Aq. NaOH (1 eq.)</td>
<td>2a</td>
</tr>
</tbody>
</table>
Next we focused on achieving this conversion in one pot starting from 3-chloropropenals. For this first we converted 3-chloropropenals to chloropropenenitriles adopting our previously developed methodology employing I$_2$ and aq. ammonia in dichloromethane as solvent. After complete conversion of starting material as evident by TLC, the solvent was evaporated on rotary evaporator. THF was added to dissolve the solid residue left in the flask followed by addition of aqueous NaOH (1 eq.) solution which successfully led to the formation of propynenitriles. After optimization of protocol for one pot preparation of propynenitrile from 3-chloropropenals, we synthesized 17 differently substituted propynenitriles (Table 5.2).

**Table 5.2.** One pot methodology for the formation of propynenitriles from chloropropenales and study of substrate scope.

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Reactants</th>
<th>Intermediate(s) (Z:E)</th>
<th>Product(s)</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td><img src="Ar" alt="" />ClCHO</td>
<td><img src="Ar" alt="" />ClCN</td>
<td><img src="Ar" alt="" />≡CN</td>
<td>78 %</td>
</tr>
<tr>
<td>2.</td>
<td><img src="H" alt="" />ClCHO</td>
<td><img src="H" alt="" />ClCN</td>
<td><img src="H" alt="" />≡CN</td>
<td>82 %</td>
</tr>
<tr>
<td>3.</td>
<td><img src="H" alt="" />OC<img src="H" alt="" />ClCHO</td>
<td><img src="H" alt="" />OC<img src="H" alt="" />ClCN</td>
<td><img src="H" alt="" />OC<img src="H" alt="" />≡CN</td>
<td>89 %</td>
</tr>
<tr>
<td>4.</td>
<td><img src="F" alt="" />ClCHO</td>
<td><img src="F" alt="" />ClCN</td>
<td><img src="F" alt="" />≡CN</td>
<td>84 %</td>
</tr>
<tr>
<td>Sr. No.</td>
<td>Reactants</td>
<td>Intermediate(s) (Z:E)</td>
<td>Product(s)</td>
<td>Yield</td>
</tr>
<tr>
<td>-------</td>
<td>-----------</td>
<td>-----------------------</td>
<td>------------</td>
<td>-------</td>
</tr>
<tr>
<td>5.</td>
<td><img src="1e" alt="image" /></td>
<td><img src="2e" alt="image" /> (100:0)</td>
<td><img src="3e" alt="image" /></td>
<td>91 %</td>
</tr>
<tr>
<td>6.</td>
<td><img src="1f" alt="image" /></td>
<td><img src="2f" alt="image" /> (100:0)</td>
<td><img src="3f" alt="image" /></td>
<td>88 %</td>
</tr>
<tr>
<td>7.</td>
<td><img src="1g" alt="image" /></td>
<td><img src="2g" alt="image" /> (100:0)</td>
<td><img src="3g" alt="image" /></td>
<td>88 %</td>
</tr>
<tr>
<td>8.</td>
<td><img src="1h" alt="image" /></td>
<td><img src="2h" alt="image" /> (100:0)</td>
<td><img src="3h" alt="image" /></td>
<td>84 %</td>
</tr>
<tr>
<td>9.</td>
<td><img src="1i" alt="image" /></td>
<td><img src="2i" alt="image" /> (100:0)</td>
<td><img src="3i" alt="image" /></td>
<td>87 %</td>
</tr>
<tr>
<td>10.</td>
<td><img src="1j" alt="image" /></td>
<td><img src="2j" alt="image" /> (100:0)</td>
<td><img src="3j" alt="image" /></td>
<td>89 %</td>
</tr>
<tr>
<td>11.</td>
<td><img src="1k" alt="image" /></td>
<td><img src="2k" alt="image" /> (46:54)</td>
<td><img src="3k" alt="image" /></td>
<td>32 %</td>
</tr>
<tr>
<td>12.</td>
<td><img src="1l" alt="image" /></td>
<td><img src="2l" alt="image" /> (75:25)</td>
<td><img src="3l" alt="image" /></td>
<td>63 %</td>
</tr>
<tr>
<td>Sr. No.</td>
<td>Reactants</td>
<td>Intermediate(s) ((Z:E))</td>
<td>Product(s)</td>
<td>Yield</td>
</tr>
<tr>
<td>--------</td>
<td>-----------</td>
<td>----------------------------</td>
<td>------------</td>
<td>-------</td>
</tr>
<tr>
<td>13.</td>
<td>(\text{Cl}-\text{C}H\text{O}\text{Cl}) (\text{CHO}) (1m)</td>
<td>(\text{Cl}-\text{C}H\text{O}\text{Cl}) (\text{C}N) (2m) ((100:0))</td>
<td>(\text{Cl}-\text{C}H\text{O}\text{Cl}) (\text{C}N) (3m)</td>
<td>85 %</td>
</tr>
<tr>
<td>14.</td>
<td>(\text{Cl}-\text{C}H\text{O}\text{Cl}) (\text{CHO}) (1n)</td>
<td>(\text{Cl}-\text{C}H\text{O}\text{Cl}) (\text{C}N) (2n) ((57:43))</td>
<td>(\text{Cl}-\text{C}H\text{O}\text{Cl}) (\text{C}N) (3n)</td>
<td>46 %</td>
</tr>
<tr>
<td>15.</td>
<td>(\text{Cl}-\text{C}H\text{O}\text{Cl}) (\text{CHO}) (1o)</td>
<td>(\text{Cl}-\text{C}H\text{O}\text{Cl}) (\text{C}N) (2o) ((100:0))</td>
<td>(\text{Cl}-\text{C}H\text{O}\text{Cl}) (\text{C}N) (3o)</td>
<td>85 %</td>
</tr>
<tr>
<td>16.</td>
<td>(\text{Cl}-\text{C}H\text{O}\text{Cl}) (\text{CHO}) (1p)</td>
<td>(\text{Cl}-\text{C}H\text{O}\text{Cl}) (\text{Cl}-\text{C}H\text{O}\text{Cl}) (\text{C}N) (2p) ((100:0))</td>
<td>(\text{Cl}-\text{C}H\text{O}\text{Cl}) (\text{C}N) (3p)</td>
<td>83 %</td>
</tr>
<tr>
<td>17.</td>
<td>(\text{OH}-\text{C}H\text{O}\text{Cl}) (\text{CHO}) (1q)</td>
<td>(\text{NC}-\text{C}H\text{O}\text{Cl}) (\text{Cl}-\text{C}H\text{O}\text{Cl}) (\text{C}N) (2q) ((100:0))</td>
<td>(\text{Cl}-\text{C}H\text{O}\text{Cl}) (\text{C}N) (3q)</td>
<td>79 %</td>
</tr>
</tbody>
</table>

It is noteworthy to mention here that when differently substituted arylchloropropenenitriles were subjected under the basic conditions, only Z-isomers of alkenes underwent elimination reaction leading to the formation of corresponding propynenitriles while E-isomers were not converted to propynenitriles and remained as such. Since replacing aromatic ring by 1-naphthyl, \(o\)-Cl-phenyl and \(o\)-OCH\(_3\)-phenyl lead to formation of both \(E\) and \(Z\) isomers of chloropropenenitriles, a mixture of propynenitriles and unreacted \(E\)-isomer of chloropropenenitrile were obtained in all these three cases. The fact that only \(Z\)-isomers (H and Cl are trans to each other) were
converted to alkynenitriles, helped us to propose a plausible mechanism for this conversion as given in Scheme 5.23.

\[
\begin{align*}
\text{Scheme 5.23}
\end{align*}
\]

5.3. Conclusions

In view of synthetic importance of alkynenitriles, many elegant methodologies have been reported in literature. But use of cyanide based cyanating agents, formation of side products and tedious reaction procedure limits their practical applicability. We have developed an efficient and facile approach to prepare conjugated alkynenitriles in one pot manner directly from 3-chloroacrylaldehydes using molecular iodine, aqueous ammonia and sodium hydroxide. Use of non-toxic reagents and economically benign aqueous reaction conditions make our methodology superior to the existing ones. It is also noteworthy that no side products are formed, yield of the reaction is excellent and products formed do not need further purification.
5.4. Experimental section

Melting points were determined in open glass capillaries in an electrical melting point apparatus and are uncorrected. The infrared (IR) spectra were recorded on Shimadzu-21 FT-IR or Perkin Elmer IR Spectrophotometer using the KBr pellet technique. $^1$H NMR and $^{13}$C NMR spectra were recorded in pure DMSO-d$_6$ on Bruker NMR spectrometers at 300/400 MHz and 75.5/100 MHz respectively using tetramethylsilane (TMS) as internal standard. Chemical shifts are expressed in $\delta$ ppm. Mass spectra (DART-MS) were recorded on a JEOL-AccuTOFJMS-T100LC Mass spectrometer having a DART (Direct Analysis in Real Time) source in ES$^+$ mode. The purity of the compounds was checked by $^1$H NMR and thin layer chromatography (TLC) on silica gel plates using a mixture of petroleum ether and ethyl acetate as eluent. UV lamp was used as a visualizing agent. Abbreviations's' for singlet, ‘d’ for doublet, ‘dd’ for doublet of doublet, ‘m’ for multiplet, ‘ex’ for exchangeable proton are used for NMR assignments; ‘s’ for strong, ‘m’ for medium for IR and ‘br’ for broad in NMR as well as IR assignments. ‘d’ stands for decomposition in melting point data.

5.4.1. Typical experimental procedure for conversion of $\beta$-chloropropenals into $\beta$-chloropropenenitriles using molecular iodine and aqueous ammonia

To a stirring solution of 3-chloropropenal (1, 1.00 mmol) in 10 ml of dichloromethane added molecular iodine (1.00 mmol) followed by addition of 2 ml of 30% aqueous ammonia solution. The reaction mixture was allowed to stir further for 45 minutes when whole solution became almost colourless showing the complete consumption of iodine. Excess of iodine was neutralized with aqueous sodium thiosulphate solution and the organic layer was evaporated under reduced pressure. THF was then added to dissolve the solid mass left followed by addition of aqueous NaOH solution. The reaction mixture was further allowed to stir for 15 min. when the TLC showed complete consumption of reactant. Whole reaction mixture was then added to water and resulting solid was filtered off, dried and recrystallized from a mixture of ethylacetate and pet ether.
3-phenyl-2-propynenitrile (3a)\textsuperscript{16}
Yield: 78 %; m.p. 36-37 °C; IR(KBr) cm\textsuperscript{-1}: 3040 (aromatic C-H stretch), 2269 (C≡N stretch), 2145 (C≡C stretch); \textsuperscript{1}H-NMR (300 MHz, CDCl\textsubscript{3}): δ 7.60 (t, J = 7.2 Hz, 2H, Ar), 7.54 (d, J = 7.2 Hz, 1H, Ar), 7.43 (t, J = 7.2 Hz, 2H, Ar); \textsuperscript{13}C NMR (75.5 MHz, CDCl\textsubscript{3}): δ 133.5, 131.9, 128.9, 117.4, 105.4, 83.0, 63.0.

3-(4-methylphenyl)-2-propynenitrile (3b)\textsuperscript{5}
Yield: 82 %; m.p. 53 °C; IR(KBr) cm\textsuperscript{-1}: 3040 (aromatic C-H stretch), 2260 (C≡N stretch), 2145 (C≡C stretch); \textsuperscript{1}H-NMR (400 MHz, CDCl\textsubscript{3}): δ 7.49 (d, J = 8 Hz, 2H, Ar), 7.21 (d, J = 8 Hz, 2H, Ar), 2.40 (s, 3H, CH\textsubscript{3}); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): δ 142.9, 133.5, 129.7, 129.5, 114.4, 105.7, 83.6, 62.8, 21.9 (CH\textsubscript{3}).

3-(4-methoxyphenyl)-2-propynenitrile (3c)\textsuperscript{16}
Yield: 89 %; m.p. 77 °C; IR(KBr) cm\textsuperscript{-1}: 3070 (aromatic C-H stretch), 2253 (C≡N stretch), 2137 (C≡C stretch); \textsuperscript{1}H-NMR (400 MHz, CDCl\textsubscript{3}): δ 7.55 (d, J = 6.8 Hz, 2H, Ar), 7.21 (d, J = 6.8 Hz, 2H, Ar), 3.85 (s, 3H, OCH\textsubscript{3}); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): δ 162.4, 135.5, 114.7, 109.2, 105.9, 83.8, 62.5, 55.64.

3-(4-fluorophenyl)-2-propynenitrile (3d)\textsuperscript{16}
Yield: 84 %; m.p. 64 °C; IR(KBr) cm\textsuperscript{-1}: 3070 (aromatic C-H stretch), 2260 (C≡N stretch), 2145 (C≡C stretch); \textsuperscript{1}H-NMR (400 MHz, CDCl\textsubscript{3}): δ 7.64-60 (m, 2H, Ar), 7.13-7.09 (m, 2H, Ar); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): δ 165.9, 163.4, 136.1, 136.0, 116.8, 116.6, 113.9, 113.8, 105.5, 82.0, 63.2.

3-(4-chlorophenyl)-2-propynenitrile (3e) 5
Yield: 91 %; m.p. 74 °C; IR(KBr) cm\textsuperscript{-1}: 3070 (aromatic C-H stretch), 2260 (C≡N stretch), 2145 (C≡C stretch); \textsuperscript{1}H-NMR (300 MHz, CDCl\textsubscript{3}): δ 7.56 (d, J = 8.4 Hz, 2H, Ar), 7.42 (d, J = 8.4 Hz, 2H, Ar); \textsuperscript{13}C NMR (75.5 MHz, CDCl\textsubscript{3}): δ 138.5, 134.6, 129.4, 116.0, 105.2, 81.3, 64.0.

3-(4-bromophenyl)-2-propynenitrile (3f) 5
Yield: 88 %; m.p. 79 °C; IR(KBr) cm\textsuperscript{-1}: 3090 (aromatic C-H stretch), 2260 (C≡N stretch), 2145 (C≡C stretch); \textsuperscript{1}H-NMR (300 MHz, CDCl\textsubscript{3}): δ 7.69 (d, J = 8 Hz, 2H, Ar), 7.43 (d, J = 8 Hz, 2H, Ar); \textsuperscript{13}C NMR (75.5 MHz, CDCl\textsubscript{3}): δ 138.5, 134.6, 129.4, 116.0, 105.2, 81.3, 64.0.
C-H stretch), 2260 (C≡N stretch), 2137 (C≡C stretch); \(^1\)H-NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.56 (d, \(J = 8.8\) Hz, 2H, Ar), 7.46 (d, \(J = 8.8\) Hz, 2H, Ar); \(^13\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 134.8, 132.4, 127.1, 116.5, 105.4, 81.9, 64.2\).

3-(4-nitrophenyl)-2-propynenitrile (3g)\(^33\)

Yield 88 %; m. p. 140 °C; IR(KBr) cm\(^{-1}\): 3109 (aromatic C-H stretch), 2361 (C≡N stretch), 2276 (C≡C stretch); \(^1\)H-NMR (300 MHz, CDCl\(_3\)): \(\delta = 8.31\) (d, \(J = 9.0\) Hz, 2H, Ar), 7.82 (d, \(J = 9.0\) Hz, 2H, Ar); \(^13\)C NMR (75.5 MHz, CDCl\(_3\)): \(\delta = 149.2, 134.5, 123.9, 104.6, 79.8, 66.6\).

3-(3-bromophenyl)-2-propynenitrile (3h)

Yield: 84 %; m. p. 73 °C; IR(KBr) cm\(^{-1}\): 3070 (aromatic C-H stretch), 2361 (C≡N stretch), 2260 (C≡C stretch); \(^1\)H-NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.66-7.75\) (m, 1H, Ar), 7.65-7.67 (m, 1H, Ar), 7.54 (dt, \(J = 8.0\) & 1.2 Hz, 1H, Ar), 7.29 (d, \(J = 8.0\) Hz, 1H, Ar); \(^13\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 136.0, 135.2, 132.1, 130.4, 122.7, 119.6, 105.2, 81.1, 64.1\).

3-(3-nitrophenyl)-2-propynenitrile (3i)\(^33\)

Yield: 87 %; m. p. 82 °C; IR(KBr) cm\(^{-1}\): 3086 (aromatic C-H stretch), 2260 (C≡N stretch), 2145 (C≡C stretch); \(^1\)H-NMR (400 MHz, CDCl\(_3\)): \(\delta = 8.47\) (t, \(J = 2\) Hz, 1H, Ar), 8.37-8.40 (m, 1H, Ar), 7.93 (d, \(J = 8.0\) Hz, 1H, Ar), 7.66 (t, \(J = 8.0\) Hz, 1H, Ar); \(^13\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 148.3, 138.9, 130.4, 128.4, 126.6, 119.6, 104.8, 79.9, 65.1\).

3-(3,4-dichlorophenyl)-2-propynenitrile (3j)

Yield: 89 %; m. p. 72 °C; IR(KBr) cm\(^{-1}\): 3086 (aromatic C-H stretch), 2268 (C≡N stretch), 2145 (C≡C stretch); \(^1\)H-NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.69\) (d, \(J = 2.0\) Hz, 1H, Ar), 7.50 (d, \(J = 8.8\) Hz, 1H, Ar), 7.44 (dd, \(J = 8.0, 2.0\) Hz, 1H, Ar); \(^13\)C NMR (75.5 MHz, CDCl\(_3\)): \(\delta = 137.2, 134.9, 133.7, 132.4, 131.2, 117.5, 105.0, 80.2, 64.7\).

3-(2-chlorophenyl)-2-propynenitrile (3k)\(^28\)

Yield: 32 %; m. p. 61 °C; IR(KBr) cm\(^{-1}\): 3086 (aromatic C-H stretch), 2271 (C≡N stretch), 2145 (C≡C stretch); \(^1\)H-NMR (300 MHz, CDCl\(_3\)): \(\delta = 7.61\) (d, \(J = 7.5\) Hz, 1H, Ar), 7.38-7.49 (m, 3H, Ar).
3-(2-methoxyphenyl)-2-propynenitrile (3l)\textsuperscript{28}

Yield: 63\%; m. p. 63 °C; IR(KBr) cm\textsuperscript{-1}: 3086 (aromatic C-H stretch), 2271 (C≡N stretch), 2145 (C≡C stretch); \textsuperscript{1}H-NMR (300 MHz, CDCl\textsubscript{3}): δ 7.46-7.55 (m, 2H, Ar), 6.93-7.00 (m, 2H, Ar), 3.92 (s, 3H, OCH\textsubscript{3}); \textsuperscript{13}C NMR (75.5 MHz, CDCl\textsubscript{3}): δ 162.9, 135.2, 133.4, 120.7, 111.0, 106.9, 105.7, 80.3, 66.6, 55.8 (OCH\textsubscript{3}).

3-[1,1'-biphenyl]-4-yl-2-propynenitrile (3m)

Yield: 85\%; m. p. 67 °C; IR(KBr) cm\textsuperscript{-1}: 3063 (aromatic C-H stretch), 2361 (C≡N stretch), 2260 (C≡C stretch); \textsuperscript{1}H-NMR (400 MHz, CDCl\textsubscript{3}): δ 7.59-7.69 (m, 6H, Ar), 7.41-7.51(m, 3H, Ar); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): δ 144.7, 139.4, 134.0, 129.1, 128.6, 127.5, 127.2, 116.1, 105.6, 83.2, 63.7.

3-(1-naphthyl)-2-propynenitrile (3n)\textsuperscript{28}

Yield: 46\%; m. p. 52 °C; IR(KBr) cm\textsuperscript{-1}: 3063 (aromatic C-H stretch), 2253 (C≡N stretch), 2145 (C≡C stretch); \textsuperscript{1}H-NMR (300 MHz, CDCl\textsubscript{3}): δ 8.19 (s, 1H, Ar), 7.84-7.87 (m, 3H, Ar), 7.54-7.63 (m, 3H, Ar); \textsuperscript{13}C NMR (75.5 MHz, CDCl\textsubscript{3}): δ 134.3, 133.8, 132.9, 132.6, 128.8, 128.3, 127.3, 125.1, 125.0, 115.0, 105.6, 81.8, 67.3.

3-(2-naphthyl)-2-propynenitrile (3o)

Yield: 85\%; m. p. 62 °C; IR(KBr) cm\textsuperscript{-1}: 3063 (aromatic C-H stretch), 2253 (C≡N stretch), 2137 (C≡C stretch); \textsuperscript{1}H-NMR (300 MHz, CDCl\textsubscript{3}): δ 8.19 (s, 1H, Ar), 7.84-7.87 (m, 3H, Ar), 7.54-7.63 (m, 3H, Ar); \textsuperscript{13}C NMR (75.5 MHz, CDCl\textsubscript{3}): δ 135.5, 134.1,132.5, 128.9, 128.8, 128.3, 128.1, 127.9, 127.6, 114.7,105.7, 83.6, 63.3.

3-[3-(3-nitriolo-1-propynyl)phenyl]-2-propynenitrile (3p)

Yield: 83\%; m. p. 69 °C; IR(KBr) cm\textsuperscript{-1}: 3063 (aromatic C-H stretch), 2288 (C≡N stretch), 2145 (C≡C stretch); \textsuperscript{1}H-NMR (400 MHz, CDCl\textsubscript{3}): δ 7.84 (d, J = 1.2 Hz, 1H), 7.75 (dd, J = 8.0, 1.2 Hz, 2H), 7.51 (t, J = 8.0, 1H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): δ 137.9, 136.3, 129.8, 119.1, 105.0, 80.3, 64.7.
3-[4-(3-nitriilo-1-propynyl)phenyl]-2-propynenitrile (3q) \(^{33}\)

Yield: 79 %; m. p. 66 °C; IR(KBr) cm\(^{-1}\): 3063 (aromatic C-H stretch), 2361 (C≡N stretch), 2288 (C≡C stretch); \(^1\)H-NMR (300 MHz, CDCl\(_3\)): δ 7.65 (s, 4H, Ar); (75.5 MHz, CDCl\(_3\)): δ 133.8, 121.1, 105.0, 80.9, 66.3.
5.5. References