Direct cyanation, hydrocyanation, dicyanation and cyanofunctionalization of alkynes

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In this review, direct cyanation, hydrocyanation, dicyanation, cyanofunctionalization and other cyanation reactions of alkynes were highlighted. Firstly, the use of nitriles and development of cyanation was simply introduced. After presenting the natural properties of alkynes, cyanation reactions of alkynes were classified and introduced in detail. Transition metal catalysed direct cyanation and hydrocyanation of alkynes gave alkynyl cyanides and alkenyl nitriles in good yields. Dicyanation of alkynes produced 1,2-dicyano adducts. Cyanofunctionalization of alkynes afforded functional cyanated compounds. Thiocyanation and selenocyanation yielded the expected functional vinylthiocyanates and vinylselenocyanates. A plausible reaction mechanism is presented if available.

Introduction

The nitrile group, an equivalent to carbonyl, carboxyl, amino and hydroxymethyl groups, has been considered as not only a key building block in many pharmaceuticals and bioactive compounds but also an important and versatile group that can be easily transformed into various derivatives such as nitrogen-containing heterocycles, amides, amines and so on. Meanwhile, nitriles, occurring in lots of natural products and important precursors for amides, amines, esters, carboxylic acids, ketones, aldehydes and alcohols, are versatile intermediates for the preparation of pharmaceuticals, pesticides and organic materials. For example, acrylonitrile is an important monomer for manufacture of plastics, rubbers, fiber, agrochemicals and pharmaceutical, while cyanamides have been widely used as ambidentate ligands in coordination chemistry. Nitriles could be readily obtained by traditional cyanation reactions including Sandmeyer reaction, Rosenmud-von Braun reaction, and other transition-metal catalyzed cyanation reactions applying metal cyanides or metalloid cyanides as cyanide source. But these above protocols usually used toxic metal cyanation reagents and also required prefunctionalization of these cyanation reagents. According to the 12 principles of green chemistry, a green chemical process should avoid the use of toxic reagents. Thus, many less toxic or green cyanation reagents were discovered, including safe reagent 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), benzyl cyanide, acetonitrile, N,N-dimethylformamide (DMF), azobisisobutyronitrile (AIBN), trimethylsilylcyanide (TMSCN), ary(cyano)iodonium triflates, N-cyano-N-phenyl-p-toluenesulfonamide (NCTS), bis(dialkylamino)cyanoboranes, malononitrile, and so on.

Alkynes are fundamentally useful unsaturated compounds which are omnipresent in many natural products, and pharmaceuticals, agrochemicals and organic materials because of their unique physical, chemical and biological properties. And inherently nucleophilic alkynes are also important intermediates in organic synthesis for preparation of biological active compounds and organic functional compounds used in organic field-effect transistors, organic light-emitting diodes, liquid crystals and dye-sensitised solar cells. Direct cyanation, hydrocyanation, dicyanation and cyanofunctionalization of alkynes, useful protocols for synthesis of interesting nitriles such as acrylonitriles, alkynyl cyanides, dicyano-substituted and cyanofunctionalized derivatives, have attracted more and more attention. In this review, direct cyanation, hydrocyanation, dicyanation and cyanofunctionalization of alkynes are presented. Numerous less toxic or green cyanation reagents are efficient for direct cyanation, hydrocyanation, dicyanation and cyanofunctionalization of alkynes.

Direct cyanation and hydrocyanation of alkynes

In 2013, Okamoto and Ohe reported copper catalysed cyanation of terminal alkynes with cyanogen iodide (ICN). When CuOTf-toluene was applied as a catalyst and tetramethylpiperidine (TEMP) was used as a base, direct cyanation of terminal acetylene 1 with ICN proceeded smoothly and gave the desired alkynyl cyanides 2 in moderate to good yields (Scheme 1).
Cu-catalyzed direct cyanation of terminal alkynes with AMBN (azobisisoamylonitrile) or AIBN (azobisisobutyronitrile) was demonstrated by Mao and Xu in 2015. As shown in Scheme 2, the desired alkenyl cyanides 4 were obtained in 45–92% yield when terminal acetylene 3 was treated with AMBN and Cu(OAc)$_2$ in acetonitrile at 80 °C under air. While under argon atmosphere, the direct cyanation of terminal alkynes 5 with AIBN occurred and gave the desired addition products isobutyronitriles 6 in moderate yields. The above direct cyanation reactions of terminal alkynes with AMBN or AIBN had remarkable advantages including a less toxic cyanation reagent and wide substrate scope.

Silver-mediated direct cyanation of terminal alkynes for the synthesis of propionitrile derivatives had been achieved by Wang and Bi. Direct cyanation reaction of terminal alkynes 7 with N-isocyanomethyltriphenylphosphorane (NIITP) in the presence of a quantitative amount of AgOTf in DMF produced propionitriles 8 in moderate to good yields (Scheme 3).

A plausible mechanism for this cyanation reaction was shown in Scheme 4, firstly, ethynylbenzene reacted with AgOTf to generate the silver acetylide A. Then, an acetylenic imido complex B was produced by insertion of NIITP into the silver-carbon bond of A. Finally, the complex B converted to target 3-phenylpropionitrile with the release of AgOH and triphenylphosphine azaylide. This procedure, applying NIITP as a nontoxic, facile “CN” source, was characterized by its operational simplicity, high efficiency with excellent yields, broad substrate scope, and greater functional group tolerance.

In addition, copper-catalyzed direct cyanation of terminal alkynes with benzoyl cyanide was reported by Li in 2018. This protocol using less toxic, stable and easy to handle benzoyl cyanide as a cyanide source and air as an oxidant provided a good alternative to the preparation of 3-arylpropionitriles under mild condition.

The first highly stereo- and regioselective hydrocyanation of terminal alkynes with acetone cyanohydrin was reported by Ritter. Treatment of aromatic terminal alkynes 9 with acetone cyanohydrin, dpff, and TpRh(COD) (Tp = (tris(1-pyrazolyl)borohydride)) in CH$_3$CN and heating at 110 °C afforded the desired anti-Markovnikov alkyn-enitriles 10 in 51–88% yield without the formation of Markovnikov product. Instead of dpff, DPE-phos enabled facile hydrocyanation of aliphatic terminal alkynes with acetone cyanohydrin. Mixing of aliphatic terminal alkynes 11, acetone cyanohydrin, DPE-phos, and TpRh(COD) (Tp = (tris(1-pyrazolyl)borohydride)) in CH$_3$CN and heating at 110 °C afforded the desired alkyn-enitriles 12 in 62–85% yield with the ratio of anti-Markovnikov products (a-M) to Markovnikov products (M) from 4 : 1 to 20 : 1 (Scheme 5).

The first efficient and general nickel catalyzed hydrocyanation of terminal alkynes with Zn(CN)$_2$ was developed by Liu in 2018. When water was used as a hydrogen source, Ni(acac)$_2$ was applied as a catalyst and Mn was employed as an additive, hydrocyanation of terminal aryl alkynes 13 with Zn(CN)$_2$ proceeded smoothly to afford the desired Markovnikov addition products 14 in moderate to good yields. Under the above standard reaction conditions of aryl alkynes, the hydrocyanation reactions of terminal aliphatic alkynes with Zn(CN)$_2$ did not proceed completely. While addition of neocuproine as ligand finished the desired functionalized vinyl nitriles 16 in 60–83% yields (Scheme 6). This protocol, avoiding use of the volatile and hazardous reagent like HCN, offered
a regioselective method for preparation of functionalized vinyl nitriles with a range of structural diversity under mild reaction conditions.\(^\text{27}\)

A reaction mechanism for the above hydrocyanation of terminal alkynes with Zn(CN)\(_2\) was tentatively proposed. As depicted in Scheme 7, firstly, reduction of Ni(acac)\(_2\) with Mn formed Ni(0) species. Then Ni(0) intermediate \(C\) was generated by oxidative addition of water to Ni(0). The alkenyl nickel complex \(D\) was produced by insertion of alkyne to \(C\) via \(\text{cis}\)-addition of Ni–H bond (hydronickelation). Possibly, the stability of the alkenyl nickel species influenced the regioselectivity of this step. The desired nitriles was formed via transmetalation of \(D\) with Zn(CN)\(_2\) followed by reductive elimination. Alternatively, the same intermediate \(D\) could be also afforded by reaction of nickel \(\pi\)-alkyne complex \(F\) with H\(_2\)O. The detailed process for this transformation was not clear yet, it may proceed through oxidative addition of water with \(F\) or cleavage of nickel-acycloprenne intermediate \(G\) by water.\(^\text{27}\)

In 2019, Yang and Chang reported the first example of Ni-mediated dehydration of formamide to form “CN” and its subsequent catalytic applications in the hydrocyanation of alkynes (Scheme 8). Treatment of acetylenes 17 and formamide with Ni(acac)\(_3\)/Co(acac)\(_2\)/Xantphos catalytic system gave the corresponding products 19 in 70–96%. The above reaction generated “CN” unit from readily available nontoxic organic precursors via nickel catalysis, was an efficient protocol for synthesis of vinyl nitriles.\(^\text{28}\)

In the same year, Lan and Xiao demonstrated the first asymmetric propargylic radical cyanation via a synergetic photoredox/copper catalysis strategy. After irradiating acetylenes 20 and trimethylsilyl cyanide (TMSCN) with visible light (2 × 3 W, purple LEDs, 390 nm) for 24 h in the presence of organic photocatalyst Ph-PTZ, catalyst Cu(MeCN)\(_2\)BF\(_4\) and chiral bisoxazoline (box) ligand \(L’\), the desired propargyl cyanide products 21 was detected in moderate to excellent yields with 83–98% ee. The above strategy, providing an unprecedented access to optically enriched propargyl cyanides with generally high reaction efficiency and enantioselectivity under mild conditions, not only offered a new way for catalytic asymmetric propargylic functionalization, but also provided a novel dual catalysis system for visible-light-induced asymmetric chemical bond formation (Scheme 9).\(^\text{29}\)

### Dicyanation of alkynes

In 2009, Arai reported a palladium(II) catalysed stereoselective 1,2-dicyanation of various alkynes with TMSCN under aerobic conditions. Treatment of alkynes 22 with PdCl\(_2\), TMSCN and O\(_2\) in toluene gave the corresponding 1,2-dicyano adducts 23 in 50–82% yields (Scheme 10).\(^\text{30}\)

The same research group investigated palladium catalysed dicyanation \([4 + 2]\) cycloaddition of various ene–ynes. As shown in Scheme 11, Pd(CN)\(_2\) catalysed 1,2-dicyanation of alkynes 24 with TMSCN in toluene under O\(_2\) proceeded smoothly and gave a mixture of \(\text{cis}\)– and \(\text{trans}\)-adducts or trans only adducts 25 in 56–78% yields.\(^\text{31}\)

Palladium catalysed dicyanation of carbon–carbon triple bonds under aerobic conditions was also investigated. As shown in Scheme 12, subjection acetylenes 26 to PdCl\(_2\) or Pd(CN)\(_2\) catalysed dicyanation with TMSCN gave the corresponding products 27 in moderate to good yields.\(^\text{32}\) This above simple and basic method provided a new approach to 1,2-dicyano olefin.
Cyanofunctionalization of alkynes

Regio- and stereoselective chlorocyanation of alkynes was reported by Alcarazo in 2017. The reaction of alkynes 28 with thioimidazolium salt 29 in the presence of boron trichloride (BCl3) was able to provide the desired product 30 in moderate to excellent yields. The stereo- and regioselectivity observed in the above transformation was remarkable. The cyanide group was exclusively incorporated at the unsubstituted carbon atom of terminal alkynes, or at the alkyl-substituted carbon atom of 1-aryl-2-alkyl alkynes. This regioselectivity is typical for an electrophilic mechanism. In both cases, only the Z isomer was formed, thus suggesting a syn-addition pathway for the reaction (Scheme 13).

The following mechanism for the chlorocyanation reaction was proposed. Initially, Lewis adduct H which was already partially fluorinated at boron was formed by activation of the cyanating reagent 29. Vinyl cation I was generated by regioselective attack of H to the corresponding alkyne 28. The syn transfer of one chloride from boron to the carbocationic center gave iminoborane J, which then produced the desired chlorocyanated products 30 by elimination of the imidazolium–thioborane fragment (Scheme 14).

Okamoto and Ohe investigated copper catalysed regio- and stereoselective iodocyanation of alkynes with cyanogen iodide. Subjection of alkyne 31 to Cu(OAc)2 catalysed iodocyanation with ICN afforded the desired iodocyanoalkene 32 in 41–94% yields when amino-cyanation ring closure of N-(2-ethynylphenyl)-N-tosylcyanamides 33 was carried out in 1,4-dioxane with CuI as the catalyst, and Na2CO3 as the base under argon at 80 °C, and the reaction could be completed within 3 hours (Scheme 15). The plausible mechanism was proposed (Scheme 17). First, p-coordination of alkyne and nitrile moieties to the copper centre was occurred to form a substrate–copper complex K. Subsequently, the N-tosyl-2-alkynylanilide cyanocopper complex L was obtained through the heterolytic cleavage of the N–CN bond by the migration of the electrophilic cyano group to the copper centre. Transaminometalation of L across the alkyne and the following cyanation produced the desired 1-tosyl-3-cyanoindoles 34 via the intermediary of the 1-tosylindol-3-yl cyano–copper complex M. Another plausible mechanism was also proposed to start with the formation of Cu–acetylide N with the increase of π-electron density at the β-carbon. The β-cyano Cu–vinylidene complex O was formed via intramolecular nucleophilic attack of the β-carbon to the electrophilic cyanamide carbon accompanied by the N–CN bond cleavage. M was afforded by intramolecular nucleophilic attack of the remaining tosyl amide at the α-carbon of the Cu–vinylidene complex O.
Protonation of M furnished the desired product 34 and regained the Cu(I) catalyst to continue the catalytic cycle.34

A visible-light-mediated direct cyanomethylation of aryl alkynoates for synthesis of 3-cyanomethylated coumarins was demonstrated by Li in 2018. In the presence of fac-Ir(ppy)3 as a photocatalyst and NaHCO3 as a base under blue-light irradiation in acetone at room temperature, direct cyanomethylation of aryl alkynoates 35 with 2-bromoacetonitrile proceeded smoothly to afford the desired 3-cyanomethylated coumarins 36 in moderate to good yields. This reaction, using cheap and easily available bromoacetonitrile as the cyanomethylation reagent, provided a new method for synthesis of 3-cyanomethylated coumarins (Scheme 18).35

A possible reaction mechanism for the above cyanomethylation was proposed. Firstly, fac-Ir(III)(ppy)3 was irradiated to the excited state \( \text{fac-Ir}^{(\text{III})}(\text{ppy})_3^* \), which was then oxidatively quenched by BrCH2CN with the formation of a \([\text{fac-Ir}^{(\text{IV})}(\text{ppy})_3]^+\) complex and a highly reactive radical P. The radical intermediate Q, generated by addition of radical P to the triple bond of aryl alkynoates 35, underwent intramolecular spirocyclization and gave the spiroradical intermediate R. The coumarin radical T was generated by selective ester migration via a carboxyl radical S. Then, oxidation of T by \([\text{fac-Ir}^{(\text{V})}(\text{ppy})_3]^+\) formed the cyclohexadienyl cation U and regenerated fac-Ir(III)(ppy)3. Finally, the desired product 36 was produced by deprotonation of U assisted by the base (Scheme 19).35

Nickel catalysed carbocyanative cyclization of 1,6-enynes was described by Arai (Scheme 20). When acetone cyanohydrin was used as an inexpensive and easy-to-handle HCN source and Ni[P(OPh)3]2 was applied as a catalyst, carbocyanative cyclization of 1,6-enynes 37 proceeded smoothly in toluene and gave the corresponding products 38 in moderate yields.36

Sc(OTf)3 catalysed formal acylcyanation of electron-rich alkynes for synthesis of fully-substituted acrylonitriles was investigated by Zhao and Sun in 2018. The formal acylcyanation of electron-rich alkynes 39 with cyanide 40 proceeded smoothly in the presence of Sc(OTf)3 in CHCl3 under N2 and gave the corresponding ynamides, thioalkynes or ynol ethers 41 in moderate to excellent yields with remarkable Z selectivity. This reaction, featuring mild conditions, high regio- and stereo-selectivity, and a broad scope, offered an efficient protocol to fully-substituted acrylonitriles (Scheme 21).37

A plausible mechanism for the above formal acylcyanation was proposed in Scheme 22. Sc(OTf)3 could serve to activate the acynitrile by lowering its LUMO level, thereby increasing its electrophilicity and giving intermediate V. The β-carbon of the ynamide attacked the carbonyl of V followed by cyclization (i.e., \([2 + 2]\) cycloaddition) to form the oxetane intermediate W with high regioselectivity because of the high polarization of the alkyne. The desired product 42 was produced by the subsequent electrocyclic opening of the oxetane W. Conrotatory ring opening in the ring-opening process governed the syn selectivity. During the conrotatory ring opening, the CN group rotates inward, so that its \(\pi^*\) orbital can favourably interact with the breaking \(\sigma\) (C–O) orbital, thus preferentially delivering the (Z)-olefin product.37
Regio- and stereoselective cyanotriflation of alkynes using aryl(cyano)iodonium triflates was reported by Studer in 2016. When 3,5-di(trifluoromethyl)-phenyl(cyano)iodonium triflate 43 was used as the triflate and cyanide source, Fe(OAc)2 in combination with phenanthroline as the catalyst, direct vicinal alkynyl cyanotriflation of alkynes occurred with regioselective syn-addition of both the CN and OTf groups of 43 to alkynes 44 to give the desired tetrasubstituted alkenes in moderate to excellent yields. This cyanotriflation of alkynes possessed some advantages such as mild conditions, complete regioselectivity, excellent stereoselectivity, and a wide range of functional groups tolerances. And products tetrasubstituted alkenes were useful building blocks in a series of stereospecific palladium catalysed cross-coupling reactions such as Suzuki coupling, Sonogashira reaction and a Buchwald–Hartwig amidation (Scheme 23).\(^{38}\)

The CuCN-mediated cyclization–cyanation reactions of β-hydroxyalkynes and α-alkynylphenol and -aniline derivatives was developed by Pyne. Treatment of β-hydroxyalkynes or α-alkynylphenol or -aniline derivatives 46 or 48 with CuCN in DMF afforded the desired 3-cyanobenzofurans 47 or 3-cyanoindoles 49 in moderate to good yields, respectively (Scheme 24).\(^{39}\)

In 2012, Hiyama demonstrated nickel/Lewis acid catalysed polyfluoroarylcyanation of alkynes. When Ni(cod)2 was used as a catalyst and DPEphos/BPh3 was employed as a ligand, polyfluoroarylcyanation of polyfluorobenzonitriles 50 with 4-octyne proceeded smoothly and produced the desired adducts 51 in excellent yields (Scheme 25).\(^{40}\)

A plausible mechanism for the above nickel/Lewis acid catalysed polyfluoroarylcyanation of alkynes was shown in Scheme 26. The catalytic cycle should be initiated by the formation of the η²-complex Y or Z. The following oxidative addition of the C-CN bond to Ni(0) gave A’ after the cyano group nitrogen atom is bound to BPh3. Insertion of 4-octyne into the ArF-Ni bond in A’ afforded C’ via the alkynyl-coordinated complex B’. Steric repulsion between the bulkier group Pr and the polyfluorophenyl group on the Ni center in B’ was assumed to be minimal. Finally, C-C bond-forming reductive elimination of 51 from C’ generated a nickel(0) complex to complete the catalytic cycle.\(^{40}\)

Nickel catalysed hydrocyanative cyclization and three-component cross-coupling reaction between alkynes and alkynes was reported by Arai in 2013 (Scheme 27). Subjection of 52 to Me2C(OH)CN/[Ni{P(OPh3)}4]/P(OPh3) catalytic system afforded the corresponding products 53 in 43–70% yields. This protocol offered a new method for the addition of a CN functionality to C-C triple bonds and provided tetra substituted alkenes with highly regio- and stereoselective.\(^{45}\)

The possible mechanism for the above nickel catalysed hydrocyanative cyclization and three-component cross-coupling reaction between alkynes and alkynes was described in Scheme 28. Firstly, a regioselective hydronickelation of the allene occurred and generated a Ni-H species. Then, hydride attacked at the central carbon atom of the allene 52 and would give a π-
allylnickel intermediate $E'$. The following 5-exo cyclization of $E'$ gave $F'$. A subsequent elimination would give the tetrastituted alkene $F_0$ stereoselectively together with Ni$^0$. When the initial C–H bond formation occurred at the terminal allenyl carbon atom, the resulting organonickel species $G_0$ was not suitable for cyclization and produced by-products through reductive elimination. Since a cyano functionality was added exclusively to a C–C triple bond in a regio- and stereoselective fashion, it was unlikely that the two vinyl–nickel bonds in $D'$, which could be generated by the oxidative cyclization of $F'$, reacted specifically with $AC$ through protonation to give $F'$.35

Other cyanation of alkynes

In 2018, He reported ultrasound-promoted Brønsted acid ionic liquid catalysed hydrothiocyanation of activated alkynes (Scheme 29). When alkynes $55$ was treated with KSCN, BAIL-1 and water at room temperature in minimal solvent under ultrasonic radiation (40 kHz/40 W), the corresponding vinyl thiocyanates $56$ was afforded in 78–94% yields. And the catalytic system could be repeated five times without significant influence on the yield. This reaction provided an eco-friendly and practical protocol for the synthesis of Z-vinyl thiocyanates, having some features including the abundance and accessibility of raw materials, the usage of recyclable and reusable catalysts, a wide substrate scope with good to high yields, ease of scale-up and high energy efficiency.41

A plausible mechanism for the above hydrothiocyanation was proposed in Scheme 30. Firstly, a cationic intermediate $G'$ was generated by protonation of the activated alkyne with BAIL-1. Then $H'$ was further tautomerized into the zwitterionic complex $I'$. Intermediate $J'$ was produced by the nucleophilic thiocyanate ion attacked the $\beta$-carbon of intermediate $I'$. Finally, the capture of a proton dissociated from water by ultrasonic radiation proceeded from the less hindered face of intermediate $J'$, trans to SCN, thus leading to product Z-vinyl thiocyanates.41

Ultrasonic multicomponent synthesis of (Z)-$\beta$-iodo vinylthiocyanates via hydrothiocyanation of alkynes was also studied. When alkynes $57$ was treated with KSCN and I$_2$ in the presence of K$_2$S$_2$O$_8$ as the oxidant in MeCN at room temperature, the corresponding (Z)-$\beta$-iodo vinylthiocyanates $58$ was

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yielded in 82–94% yield with Z/E from 11:1 to 28:1 (Scheme 31).42

In the plausible mechanism of the above ultrasonic multicomponent synthesis of \((Z)\)-\(\beta\)-iodo vinylthiocyanates, an activated iodoirenium ion \(K'\) was formed through the molecular iodine electrophilic addition to alkyne with the release an iodine anion which was oxidized by \((\text{NH}_4)_2\text{S}_2\text{O}_8\) to regenerate \(I_2\) for continuing participation in the reaction. Then, an energetically favourable six-membered ring intermediate \(L'\) was yielded by the coordination of HOAc to intermediate \(K'\). Finally, the thio cyanate anion attacked the less steric hindered carbon atom to give the corresponding product \((Z)\)-\(\beta\)-iodo vinylthiocyanates with concomitant release of HOAc to complete the catalytic cycle (Scheme 32).42

Synthesis of a variety of \(Z\)-\(\beta\)-thiocyanate alkenyl esters via lactic acid catalysed hydrothiocyanation of alkynes was established (Scheme 33). After treating alkynes 59 with KSCN in the presence of natural lactic acid under ultrasound conditions for 30 min, the expected \(Z\)-\(\beta\)-thiocyanate alkenyl esters 60 was formed in excellent yields.43

Iodine-mediated regio- and stereoselective iodothiocyanation of alkynes was reported by Zeng and Chen in 2018 (Scheme 34). Iodothiocyanation of alkyne 61 with \(\text{NH}_4\text{SCN}\) in the presence of \(I_2\) as the iodine source and EtOH/H\(_2\)O as the solvent at 80 °C under air afforded series of functional \(\beta\)-iodo vinylthiocyanates 62 in good to excellent yields. This protocol proceeding in aqueous ethanol media under mild conditions with good functional group tolerance was a new environmentally friendly, economical and straightforward approach for versatile synthesis of vinyl thiocyanates from readily available and inexpensive \(\text{NH}_4\text{SCN}\) and \(I_2\).44

The plausible reaction pathway for the above iodothiocyanation of alkynes was shown in Scheme 35. First, an electrophilic addition of \(I_2\) to the C-C triple bond of substrate 61 led a cyclic iodonium ion \(M'\). And then, nucleophilic attack of SCN\(^{–}\) on a more substituted site of \(M'\) resulted succedent ring opening, which produced the difunctionalized product 64.44

In 2019, He investigated natural deep eutectic solvent catalysed selenocyanation of activated alkynes (Scheme 36). Under ultrasonic radiation, treatment of alkynes 63 with H\(_2\)O and KSeCN in natural deep eutectic solvent (ChCl/glycolic acid) afforded the corresponding \(Z\)-vinylselenolates 64 in 78–94% yields with \(Z/E\) ratio from 14:1 to 39:1.45

The plausible mechanism for deep eutectic solvent catalysed selenocyanation of activated alkynes was depicted in Scheme 37. First, two hydrogen bonds formed between the oxygen atom of the carboxyl group in alkynes and the H atom of the hydroxyl groups (glycolic acid) in DES, resulting in enhanced polarization of carbonyl group of alkynes (\(N'\)), which was in resonance with a zwitterionic intermediate \(O'\). Then, an intermediate \(P'\), in which a hydrogen bond formed between the nitrogen-atom of “SeCN” and the H atom of the hydroxyl group (ChCl) in ChCl/
glycolic acid, was generated by the attachment of selenocyanate anion to intermediate \( P^+ \). Finally, the intermediate \( P^+ \) captured a proton (in situ generated by ultrasound-assisted self-ionization of \( \text{H}_2\text{O} \)) on the reverse side of the sterically hindered H-bond activated atom to produce the desired Z-vinyl selenocyanates with concomitant release of the DES to fulfill the catalytic cycle.45

A green selenocyanation of activated alkynes catalysed by lactic acid was achieved by He in 2019. Treatment of a mixture of alkynes, \( \text{H}_2\text{O} \), KSeCN and lactic acid at ambient temperature under ultrasonic conditions (30 W/44 KHz/25–32 °C) in open air led to the expected Z-3-selenocyanatoacrylates and analogues in excellent yields. This protocol, using a minimal amount of lactic acid as reaction media, entirely avoided the usage of organic volatile compounds. And the reaction also had other advantages such as the conversion of substrate was almost quantitative, the pure products could be conveniently collected through water precipitation and the cheap biomass lactic acid could be re-used for five consecutive runs without obvious decrease in catalytic activity (Scheme 38).46

Scheme 36 Deep eutectic solvent catalysed selenocyanation of activated alkynes.

Scheme 37 Plausible mechanism for deep eutectic solvent catalysed selenocyanation of activated alkynes.

Scheme 38 Green selenocyanation of activated alkynes catalysed by lactic acid.

Stereoselective difunctionalization of alkynes with NaSCN or KSeCN was also reported (Scheme 39). When NaSCN was used as a [SCN] source and oxone was employed as an oxidant, dithiocyanation of alkynes 67 proceeded smoothly in DCM and produced the desired alkenyl dithiocyanates 68 in 72–87% yield. The expected alkenyl diselenocyanates 69 was obtained in good yield when alkynes 67 was treated with KSeCN [SeCN] source and PhI(OAc)₂ oxidant in \( \text{H}_2\text{O} \).

A possible mechanism for the difunctionalization of alkynes was proposed in Scheme 40. Firstly, in the presence of an oxidant oxone or PhI(OAc)₂, NaSCN or KSeCN was converted into the SCN radical \( Q^+ \) or the SeCN radical \( S^+ \). Then, the anti-Markovnikov addition of \( Q^+ \) or \( S^+ \) to alkyn 67 produced the alkenyl radical \( R^+ \) or \( T^+ \). Finally, the radical \( Q^+ \) or \( S^+ \) attacked more favourably the sterically less hindered side of the alkenyl radical \( R^+ \) or \( T^+ \) which could result the formation of desired products 68 and 69, respectively.47

Conclusions

In summary, nitriles were versatile intermediates for preparation of pharmaceuticals, pesticides and organic materials. Inherently nucleophilic alkynes were important intermediates in organic synthesis for preparation of biological active compounds and organic functional compounds. Cyanation reactions of alkynes had attracted more and more attention. Transition metal catalysed direct cyanation and hydrocyanation of alkynes gave the corresponding alkyln cyanides and alkenyl nitriles in high yields. And dicyanation of alkynes could produce 1,2-dicyano adducts. Cyanofunctionalization of alkynes afforded functional cyanated compounds. Other cyanation of alkynes such as thiocyanation and selenocyanation yielded the expected functional vinylthiocyanates and vinylselenocyanates.
Limitations and perspectives

Although these above cyanation reactions were useful and convenient for synthesis of cyanates, expensive transition metal catalysts like rhodium and palladium complexes were often used to realize reasonable yields in direct cyanation of alkynes. Thus, establishment of cheap catalytic system should be focused in future research. And developing other kind cyanation of alkynes was still in high need.

Conflicts of interest

No conflict of interest exists in this paper, and the paper is approved by all authors for publication. I and my co-authors would like to declare that the work described is original and has not been published previously, and not under consideration for publication elsewhere, in whole or in part. All the authors listed have approved the contents of the paper.

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