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**PAPER**

# Per-6-amino-β-cyclodextrin/CuI catalysed cyanation of aryl halides with $K_4[Fe(CN)_6]$†

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Efficient cyanation of aryl halides is achieved using less toxic $K_4[Fe(CN)_6]$ as the reagent and amino-β-cyclodextrins as supramolecular ligands for CuI. Four different amino cyclodextrins *viz*. per-6-amino-β-CD, per-6-methylamino-β-CD, per-6-butyl-amino-β-CD and mono-6-amino-β-CD are prepared and studied. Aryl and heteroaryl nitriles are obtained in good to excellent yield for even bromo derivatives of flavone and 2-aminopyrans. This system uses catalytic amounts (10 mol%) of both copper iodide and per-6-amino-β-cyclodextrin. Easy separation, the absence of nitrogen atmosphere and excellent yield are the other significant outcomes of this protocol.

## 1. Introduction

Aryl nitriles represent an integral part of dyes, herbicides, agrochemicals, pharmaceuticals, and natural products.[1] Moreover, the nitrile group serves as an intermediate for a multitude of transformations leading to other important functional groups. Benzonitriles themselves are of significant interest, as substructures in a number of biologically active agents. Examples of pharmaceutically active benzonitriles such as bicalutamide, cyamemazine, letrozole and citalopram are well known.[2]

In spite of many synthetic methods developed for the preparation of aryl nitriles, the introduction of cyanide is the direct and most versatile route. Examples include the Rosenmund–von Braun reaction of aryl halides[3] and the diazotisation of anilines with the subsequent Sandmeyer reaction.[4] However these strategies lead to stoichiometric amounts of heavy metal waste, which has prompted research towards other methods for the preparation of aryl nitriles. Among various catalysts for the transition metal-catalysed cyanation of aryl halides, palladium compounds have been widely investigated,[5] while less expensive copper catalysts received less attention. A general problem of metal-catalyzed cyanations is the high affinity of cyanide towards Pd-, and Cu-catalysts. Often a fast deactivation of the catalytic system is observed by the formation of stable cyanide complexes and catalysis proceeds with low efficiency. To circumvent this problem the following strategies are attempted: (a) use of solvents in which cyanide sources, NaCN, KCN and $Zn(CN)_2$, are less soluble,[5b,6] (b) use of organic, for example, tetramethylenediamine,[7] and inorganic, for example, Zn and Zn salt,[8] additives to regenerate the catalytically active metal centre, (c) slow release of the corresponding cyanide source, for example acetone cyanohydrin[9] or trimethylsilyl cyanide,[10] which keeps the cyanide concentration low and leads to a higher catalyst activity. However, most of these have drawbacks such as toxicity of the cyanide source and comparably high catalyst costs.

In a significant breakthrough, Beller and co-workers reported the use of easy handling, least toxic and environmentally friendly potassium hexacyanoferrate(II) as a cyanide source in a Pd-catalysed cyanation reaction.[11,12] Involvement of all the six $CN^-$ ions of $K_4[Fe(CN)_6]$ in cyanation of aryl halides harnesses the full potential of the reagent. Also the cyanide ion is strongly bound in potassium ferrocyanide(II), warranting substantially slow release of cyanide ions which may be beneficial for reducing the inactivation of the catalyst. However, these procedures using $K_4[Fe(CN)_6]$ involve the use of expensive palladium complexes as catalysts.[13] So far, only a few cyanation reports are available with copper salts and $K_4[Fe(CN)_6]$.[14–18] The first case for copper catalysed cyanation of aryl halides using $K_4[Fe(CN)_6]$ was reported by Beller *et al.*, using $Cu(BF_4)_2{\cdot}6H_2O$/DMEDA (100 mol%).[14] Subsequently a few other catalytic systems were developed such as CuI/alkyl imidazole (200 mol%),[15] $Cu(OAC)_2{\cdot}H_2O$/ethylenediamine (100 mol%),[16] CuI-hydroxyapatite (only for aryl iodides)[17] and also using microwave conditions.[18] Though the reported procedures have many advantages, they need equimolar or more of costly/toxic ligands or microwave activation.

Cyclodextrins (CDs) are well known macrocyclic oligosaccharides possessing hydrophobic cavities that bind substrates selectively *via* noncovalent interactions.[19] Functionalization of CDs improves their properties and enhances their capability for complexation with metal ions resulting in manifold increase in their applications in catalysis.[20] Aminocyclodextrins are homogeneous CD derivatives modified by persubstitution at the primary face with amino pendant groups and this manifests

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† Electronic supplementary information (ESI) available: Spectral data of aryl nitriles and copy of spectra of NMR, ESI-MS and IR. See DOI: 10.1039/c2nj40556c

combined hydrophobic and electrostatic binding of guest molecules relative to native CDs. They are employed as biomimetic catalysts in Kemp elimination,[21a] deprotonation,[21b] and chiral recognition processes.[21c] Aminocyclodextrins are known as efficient ligands for first sphere coordination metal ions.[22] In our group, per-6-amino-β-cyclodextrin (per-6-$NH_2$-β-CD) is used extensively as a supramolecular chiral host and a base catalyst for asymmetric Michael addition of nitromethane and thiols to chalcones,[23a] Henry reaction of nitromethane to aldehydes[23b] and for the synthesis of pyranopyrazole derivatives under solvent-free conditions at room temperature.[23c] A novel, colorimetric, and ratiometric sensor is also developed for transition-metal cations $Fe^{3+}$ and $Ru^{3+}$ [23d] and phosphate/pyrophosphate anions in water,[23e] using per-6-$NH_2$-β-CD as a supramolecular host and *p*-nitrophenol as a spectroscopic probe. Recently we have reported the use of per-6-$NH_2$-β-CD as efficient ligands for the CuI catalysed *N*-arylation of imidazoles with aryl and heteroaryl bromides.[24] This prompted us to use per-6-$NH_2$-β-CD as a supramolecular ligand for copper(I) for cyanation of aryl halides with $K_4[Fe(CN)_6]$ as a cyanating agent.

## 2. Experimental section

### 2.1 Syntheses of aminocyclodextrins

**(a) Per-6-amino-β-cyclodextrin (per-6-$NH_2$-β-CD).** Per-6-$NH_2$-β-CD is synthesized and purified according to the following procedure described in the literature.[25] The product is dried for 24 h in a dryer under vacuum over phosphorous pentoxide at 60 °C and then is stored in the phosphorus pentoxide vacuum desiccator. Yield 2.35 g (91%). $^1$H-NMR (300 MHz, $D_2O$): δ H 5.14 (d, 7H), 4.15 (m, 7H), 3.97 (dd, 7H), 3.67 (dd, 7H), 3.56 (t, 7H), 3.43 (dd, 7H), 3.22 (dd, 7H); $^{13}$C-NMR (75 MHz, $D_2O$): δ C 42.8, 70.6, 74.2, 74.8, 84.8, 104.1; ESI-MS: *m*/*z*. Calcd for $C_{42}H_{77}N_7O_{28}$ is 1127.48; found 1162.53 ($M + Cl^-$ in negative mode). Elemental analysis calcd for $C_{42}H_{77}N_7O_{28}$: C, 44.72; H, 6.88; N, 8.69%. Found C, 44.59; H, 6.76; N, 8.63%.

**(b) Per-6-methylamino-β-cyclodextrin (per-6-MeNH-β-CD).** Per-6-methylamino-β-cyclodextrin is synthesized by treating per-6-iodo-6-deoxy-β-cyclodextrin with an excess of methylamine (10 molar equivalent of amine per equivalent) at 80 °C for 24–48 hours the reagent/solvent is removed under vacuum, and the residue is precipitated in acetonitrile. After filtration and washing with acetone the solid is taken up in water and the pH is carefully brought down to 4 with 1 M HCl. The aqueous solution is evaporated under vacuum and further on the vacuum line. The resulting solid is washed three times with hot absolute ethanol in order to remove all of the unreacted starting amine. The last filtrate is perfectly clear. After drying on the vacuum line, per substitution of the primary face is confirmed by NMR. Yield 1.41 g (73%). $^1$H-NMR (300 MHz, $D_2O$): δ H 5.14 (d, 7H), 4.15 (m, 7H), 3.97 (dd, 7H), 3.67 (dd, 7H), 3.56 (t, 7H), 3.43 (dd, 7H), 3.22 (dd, 7H), 3.23 (s, 3H). $^{13}$C-NMR (75 MHz, $D_2O$): δ C 31.5, 54.7, 67.7, 71.5, 72.2, 102.1; ESI-MS: *m*/*z*. Calcd for $C_{49}H_{91}N_7O_{28}$ is 1225.59; found 1226.60 (M + H in positive mode). Elemental analysis calcd for $C_{49}H_{91}N_7O_{28}$: C, 47.99; H, 7.48; N, 8.00%. Found C, 47.81; H, 7.39; N, 7.94%.

**(c) Per-6-butylamino-β-cyclodextrin (per-6-*n*-BuNH-β-CD).** Per-6-butylamino-β-cyclodextrin is synthesized by following the above procedure using butylamine. Yield 1.61 g (67%). $^1$H-NMR (300 MHz, $D_2O$): δ H 5.14 (d, 7H), 4.15 (m, 7H), 3.97 (dd, 7H), 3.67 (dd, 7H), 3.56 (t, 7H), 3.43 (dd, 7H), 3.22 (dd, 7H), 1.54 (m, 2H), 1.42 (m, 2H), 0.76 (m, 3H); $^{13}$C-NMR (75 MHz, $D_2O$): 13.1, 19.3, 27.6, 30.4, 48.7, 67.6, 71.6, 72.1, 82.1, 101.0. ESI-MS: *m*/*z*. Calcd for $C_{70}H_{133}N_7O_{28}$ is 1519.92; found 1520.91 ($M + H^+$ in positive mode). Elemental analysis calcd for $C_{70}H_{133}N_7O_{28}$: C, 55.28; H, 8.81; N, 6.45%. Found C, 55.14; H, 8.76; N, 6.39%.

**(d) Mono-6-amino-β-cyclodextrin (mono-6-$NH_2$-β-CD).** Mono-6-$NH_2$-β-CD[26] is prepared by following the literature procedures. The product is dried for 24 h under vacuum over phosphorous pentoxide at 60 °C and then stored in the same phosphorus pentoxide vacuum desiccator. Yield 2.58 g (88%). ESI-MS: *m*/*z*. Calcd for $C_{42}H_{71}NO_{34}$ is 1133.48; found 1169.50 ($M + Cl^-$ in negative mode). Elemental analysis calcd for $C_{42}H_{71}NO_{34}$: C, 44.48; H, 6.31; N, 1.24%. Found C, 44.25; H, 6.26; N, 1.19%.

### 2.2 General procedure for cyanation of aryl halides

Per-6-amino-β-cyclodextrin (0.1 mmol), aryl halide (1 mmol), CuI (0.1 mmol), $K_4[Fe(CN)_6]$ (0.2 mmol), $Na_2CO_3$ (0.2 mmol), KI (0.3 mmol) and DMF (3 mL) are taken in a Schlenk tube with a teflon stopcock. The tube is sealed and heated at 130 °C. After the reaction, the mixture is filtered, water is added to the filtrate then extracted with ethyl acetate and the organic phase is dried over $Na_2SO_4$. After evaporation of the solvents the residue is subjected to column chromatography.

## 3. Results and discussion

### 3.1 Copper catalysed cyanation of iodobenzene

Preliminary studies on cyanation of iodobenzene involve $Cu(OAc)_2 \cdot H_2O$ as the catalyst, per-6-$NH_2$-β-CD as the ligand and $K_2CO_3$ as the base. Unfortunately, the desired product is obtained in only 38% yield along with considerable amounts of phenol as a by-product. During the screening of copper salts, we found that copper sources had a significant effect on the reaction. Among the copper salts tested, copper(I) iodide is the best, and the conversion increased sharply to 98% by employing 0.3 equivalent of CuI at 130 °C in DMF for 24 h. Other copper salts, such as CuCl and $CuSO_4$ gave poor yield (27 and 13% respectively). No product was obtained in the absence of copper salts.

The nature of the ligand also dramatically influences the efficiency of the catalytic system. Reaction fails in the absence of ligand. Studies with three different aminocyclodextrins *viz*., per-6-amino-β-cyclodextrin (per-6-$NH_2$-β-CD), per-6-methylamino-β-cyclodextrin (per-6-MeNH-β-CD) and per-6-*n*-butylamino-β-cyclodextrin (per-6-*n*-BuNH-β-CD) as ligands in the above reaction (Fig. 1a) revealed that both amino and alkylaminocyclodextrins are suitable for the cyanation of aryl halides. Of this, per-6-$NH_2$-β-CD gives 98% conversion whereas per-6-methylamino-β-cyclodextrin and per-6-n-butylamino-β-cyclodextrin give 73 and 59% respectively (Fig. 1b). This indicates that as the chain length increases, the conversion

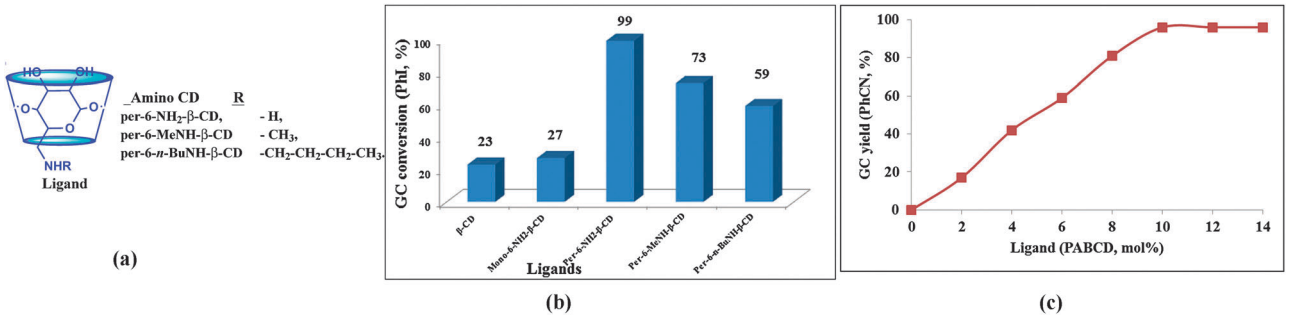



**Fig. 1** (a) Structure of aminocyclodextrins ligand. Copper catalysed cyanation of iodobenzene (b) With different ligands. (c) With different mol% of per-6-$NH_2$-β-CD. Reaction conditions: 1 mmol iodobenzene, 0.1 mmol CuI, 0.1 mmol ligand, 0.2 mmol $K_4[Fe(CN)_6]$, 0.2 mmol $Na_2CO_3$, 3 mL DMF, 130 °C for 24 h.



decreases, since the presence of alkyl groups causes steric hindrance and consequently the binding of copper(I) is affected. The reaction is also carried out with native β-CD (containing only the oxygen binding site) and mono-6-amino-β-cyclodextrin (containing both nitrogen and oxygen binding sites). In both cases, conversion (23 and 27% respectively) is lower (Fig. 1b). From these results, it is inferred that the seven amino groups present in per-6-$NH_2$-β-CD play an important role in the cyanation reaction. When the reaction is carried out in different per-6-$NH_2$-β-CD to Cu(I) ratios such as 1 : 1, 1 : 2 and 1 : 3, the conversion is 97, 97 and 98% respectively. Consequently, the subsequent reactions are carried out in a 1 : 1 per-6-$NH_2$-β-CD : CuI ratio. Further when carried out with different mol. percentages of per-6-$NH_2$-β-CD to ligand 10 mol% of the ligand is found to be optimum for carrying out the reaction (Fig. 1c).

The reaction temperature also has a very strong influence. At 80 °C, very low yield of benzonitrile is obtained. As the temperature is increased to 130 °C, conversion is increased. This can be attributed to the difficulty in the liberation of cyanide from $K_4[Fe(CN)_6]$ below 120 °C. Among the various solvents used, we found that the reaction works well when polar solvents such as DMF and DMSO are used (98 and 74%, entries 1 and 2 in Table 1). In contrast, product formation is not observed in water and less polar solvents such as toluene and acetonitrile. As *N*-methylpyrrolidine (NMP) itself forms a complex with cyclodextrin it is not used in the present study. Among the inorganic bases used, $Na_2CO_3$ afforded the best result. Interestingly, without any base, 40% yield of the product is observed (Table 1, entry 3). Organic bases show lower activity in cyanation reaction while inorganic metal carbonates acted efficiently. Other inorganic bases are less effective than carbonate bases and afforded a moderate yield of the cyanated product. The activity of the bases decreases in the following order: $Na_2CO_3 > K_2CO_3 > K_3PO_4 > Cs_2CO_3 > NaOH > Et_3N$ (Table 1, entries 1 and 4–8). In this reaction, 1.2 equivalents of $K_4[Fe(CN)_6]$ (0.2 mmol) with respect to aryl halide is used in all reactions. However, by lowering the amount of cyanide source to 0.16 mmol the conversion decreases to 87% (Table 1, entry 9).

### 3.2 Copper catalysed cyanation of aryl bromides

Reaction conditions used in the cyanation of iodobenzene are also extended to the cyanation of 5-bromopyrimidine and the cross coupling reaction gives only 23% yield. Although the result is less satisfactory, we were able to obtain good yield by using an iodide anion, which leads to catalysed production of aryl iodide from aryl bromide and its subsequent *in situ* cyanation, as reported by Buchwald *et al.*[27] The loading amount of KI was also optimised. 30 mol% of KI is sufficient to promote the cyanation of aryl bromides. Further increase or decrease in the amount of KI leads to decrease in conversion (Fig. 2a). With iodobenzene the reaction is completed in 24 h but for 5-bromopyrimidine, the reaction requires 36 h. Variation of conversion with respect to time is given in Fig. 2b.

**Table 1** Optimisation of reaction conditions[a]

| S.No | Base | Solvent | Conversion[b] |
|---|---|---|---|
| 1 | $Na_2CO_3$ | DMF | 98 |
| 2 | $Na_2CO_3$ | DMSO | 74 |
| 3 | — | DMF | 40 |
| 4 | $K_2CO_3$ | DMF | 71 |
| 5 | $Cs_2CO_3$ | DMF | 23 |
| 6 | $K_3PO_4$ | DMF | 30 |
| 7 | NaOH | DMF | 21 |
| 8 | $Et_3N$ | DMF | 17 |
| 9 | $Na_2CO_3$ | DMF | 87[c] |

[a] Reaction conditions: 1 mmol iodobenzene, 0.1 mmol CuI, 0.1 mmol per-6-$NH_2$-β-CD, 0.2 mmol $K_4[Fe(CN)_6]$, 0.2 mmol $Na_2CO_3$, 3 mL DMF, 130 °C. [b] Analysed by GC. [c] 0.16 mmol $K_4[Fe(CN)_6]$.

### 3.3 Copper catalysed cyanation of substituted aryl iodides and aryl bromides

To extend the scope of the reaction further, various aryl halides are used under the optimized conditions and the results are summarized in Table 2. Good to excellent yields are obtained for aryl iodides (entries 1–9) and aryl bromides (entries 10–21 in Table 2). In addition a wide range of functional groups such as alkyl, nitro, ester and methoxy groups are tolerated. The reaction is sensitive to the electronic effect of the substrates. Electron withdrawing aryl halides are more active than electron-rich substrates reflecting their greater electrophilicity. In general, sterically more hindered aryl halides give lesser yield. The reaction fails in 2-bromomesitylene. 2,4-Dimethoxyiodobenzene and 3,4-dimethyliodobenzene need longer reaction time to give excellent yield (entries 7 and 8). 4-Nitrobromobenzene (entry 11) gives the corresponding nitrile in excellent yield at 150 °C. At 130 °C, the yield is low (51%) and further increasing the temperature >150 °C

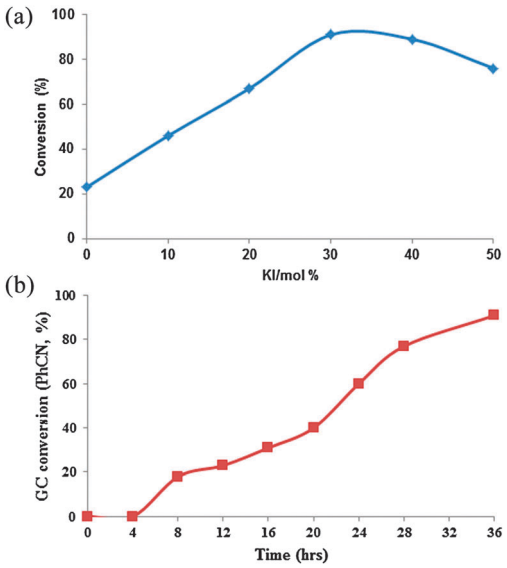



**Fig. 2** Copper catalysed cyanation of 5-bromo-pyrimidine (a) with different mol% of KI (b) with different time interval. Performed with 1 mmol 5-bromopyrimidine, 0.1 mmol CuI, 0.1 mmol per-6-$NH_2$-β-CD, 0.2 mmol $K_4[Fe(CN)_6]$, 0.2 mmol $Na_2CO_3$, 3 mL DMF, 130 °C.

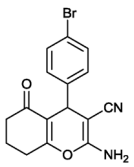
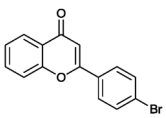
causes the reduction of the nitro group. When 4-bromoaniline is used, lesser yield (55%) is observed but good conversion is observed when the reaction is carried out after protecting the amino group with BOC anhydride. Interestingly, 2-amino-pyran (entry 20) does not require protection of the amino group. Cyanation of 4-bromochlorobenzene results in exclusive replacement of the bromo group (entry 10). Similarly, 1-cyanonaphthalene is easily obtained from 1-bromonaphthalene (entry 13).

Nitrogen containing heterocycles are difficult substrates due to their potential coordination with catalysts. Therefore, the scope of this reaction is also extended to various heterocyclic bromides such as 2-iodothiophene, 4-bromopyridine, 3-bromo-pyridine, 2-bromo-5-methylpyridine and 5-bromopyrimidine (entries 15–19). It is noteworthy to mention that most of the substrates give good to excellent yield. 4-Bromopyridine and 3-bromopyridine gave the corresponding nitriles in 71 and 69% yield, respectively, at 130 °C. For the first time, reaction is carried out in 2-aminopyrans (entry 20) and flavone (entry 21) containing a bromo group. In both cases, good yields are observed.

Cyanation of bromo group in 2-aminopyrans is significant because the product is used as positive modulators of AMPA receptors, for the treatment of neurodegenerative conditions and as cognitive enhancers.[28a] Cyanation of 4-haloflavone is done previously using the Rosenmund–von Braun reaction, which uses toxic copper(I)cyanide as a cyanating agent.[28b]

The cyanation of iodobenzene is also carried out under microwave conditions. At lower temperatures (80° and 110 °C), no reaction is observed (entries 1 and 2 in Table S2, ESI†). Reaction proceeds well only at 130 °C and after 150 min, >93% product is formed. Reaction is also carried out at different time intervals at 130 °C (entries 3–7 in Table S2, ESI†). However after 2 h, formation of 7% of a side product,

**Table 2** Aromatic cyanation of various aryl halides using $K_4[Fe(CN)_6]$ in the presence of Cu(I) and per-6-$NH_2$-β-CD[a]

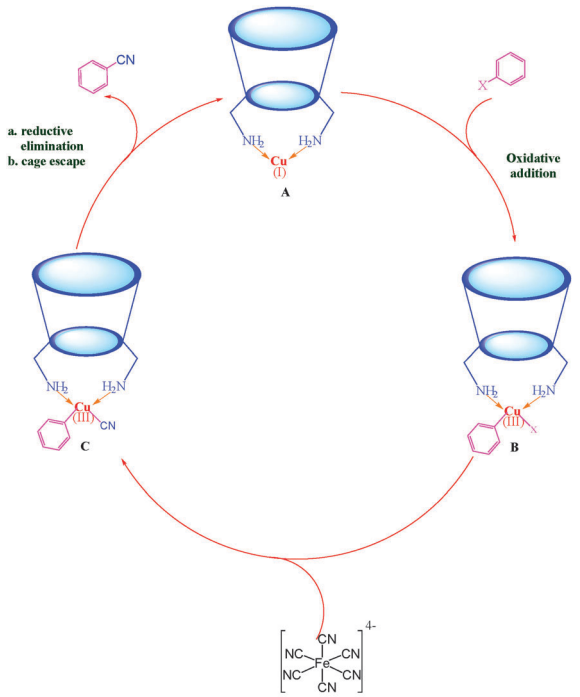
| S. No. | Aryl halide | Time (h) | Conv.[b] (%) | Yield[c] (%) |
|---|---|---|---|---|
| 1 | Iodobenzene | 24 | 97 | 95 |
| 2 | 4-Iodophenol | 24 | 99 | 89 |
| 3 | 4-Iodobenzonitrile | 18 | 100 | 97 |
| 4 | Ethyl 4-iodobenzoate | 24 | 97 | 90 |
| 5 | Ethyl 3-iodobenzoate | 24 | 85 | 79 |
| 6 | 2-Iodobenzoic acid | 24 | 79 | 76 |
| 7 | 2,4-Dimethoxyiodobenzene | 36 | 97 | 81 |
| 8 | 3,4-Dimethyliodobenzene | 36 | 94 | 83 |
| 9 | 4-Bromoiodobenzene | 24 | 93 | 79[d] |
| 10 | 4-Chlorobromobenzene | 24 | 97 | 73[e] |
| 11 | 4-Nitrobromobenzene | 24 | 98 | 87[f] |
| 12 | 4-Bromoaniline | 36 | 83 | 72[g] |
| 13 | 1-Bromonaphthalene | 36 | 81 | 73 |
| 14 | 4-(Trifluoromethoxy)-bromobenzene | 24 | 97 | 93 |
| 15 | 2-Iodothiophene | 36 | 89 | 77 |
| 16 | 4-Bromopyridine | 36 | 92 | 71 |
| 17 | 3-Bromopyridine | 36 | 76 | 69 |
| 18 | 2-Bromo-5-methylpyridine | 36 | 98 | 83 |
| 19 | 5-Bromopyrimidine | 36 | 91 | 70 |
| 20 |  | 36 | nd[h] | 81 |
| 21 |  | 36 | 93 | 73 |

[a] Reaction conditions: 1 mmol aryl halides, 0.1 mmol CuI, 0.1 mmol per-6-$NH_2$-β-CD, 0.2 mmol $K_4[Fe(CN)_6]$, 0.2 mmol $Na_2CO_3$, 3 mL DMF, 130 °C. for aryl bromides (entires 10–21) 0.3 mmol KI is added. [b] Analysed by GC. [c] Isolated yield. [d] Product is phthalonitrile. [e] Product is 4-chlorobenzonitrile. [f] At 150 °C. [g] After protection of the amino group. [h] Product is not observed in GC.

namely phenol is noticed. Further studies to optimise microwave conditions will be carried out later.

### 3.4 Mechanism of cyanation of aryl halides by per-6-$NH_2$-β-CD/CuI

A plausible three step mechanism as outlined in Scheme 1 is proposed for the per-6-$NH_2$-β-CD-CuI-catalyzed cyanation of aryl halides on the basis of literature precedents.[3c] Per-6-$NH_2$-β-CD reacts with CuI to produce a Cu-chelated complex (A) *via* interaction between amino groups of per-6-$NH_2$-β-CD and CuI. This can be supported by the observation of a strong intense peak at *m*/*z*. 1317.00 in ESI-MS (Fig. 3), which corresponds to the complex between per-6-$NH_2$-β-CD and CuI. Oxidative addition of aryl halide leads to a Cu-chelated complex generating a Cu(III) complex B, which undergoes transmetallation with $K_4[Fe(CN)_6]$ to provide a transient Cu(III) intermediate C. This leads to aryl nitriles *via* reductive elimination of Cu(III) to Cu(I). Though cyclodextrins are known to form inclusion complexes with aryl halides, in the present study it is postulated that bulk of the reaction takes place outside the CD cavity, since the reaction is facile only in DMF,




**Scheme 1** Mechanism of cyanation of aryl halides.

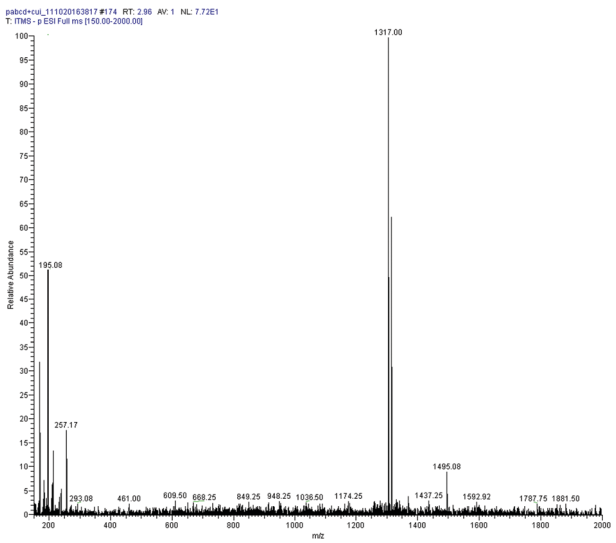



**Fig. 3** ESI-MS spectrum of per-6-$NH_2$-β-CD:CuI.

which is known to expel most of the guests from the CD cavity[29] or to considerably reduce the inclusion process. We also presumed that a small portion of the reaction might take place with aryl halide bound inside the CD cavity, as evident from the control experiment on the same reaction in the presence of adamantane (which forms a more stronger inclusion complex with CD), a decrease in conversion (36%) is noticed.

## 4. Conclusions

To conclude, herein we report for the first time copper catalysed aromatic cyanation of aryl iodides and bromides using a supramolecular ligand, per-6-amino-β-cyclodextrin. Aryl nitriles were obtained from aryl bromides through the copper catalysed *in situ* production of the corresponding aryl iodides by using catalytic amounts of potassium iodide. The significant advantages of using per-6-$NH_2$-β-CD as a ligand are (1) a catalytic amount of ligand (10 mol%) is enough to carry out the reaction to get excellent yield of aryl nitriles (previous reported procedures[15–17] need 50–200 mol% of the ligand and though a few ligand free methodologies are reported for copper,[18] they need microwave irradiation); (2) after completion of reaction, the ligand can be easily removed by simple filtration; (3) this procedure represents a more environmentally benign and less hazardous protocol using the less-toxic potassium hexacyanoferrate(II) as a cyanating agent; (4) due to the slow release of cyanide ions, its binding to Cu(I) is markedly slower compared to the previously known procedure and this enhances profoundly the efficiency of the catalyst; (5) this method avoids an inert atmosphere, which is a common requisite with earlier works; (6) for the first time the bromo group present in flavone and 2-aminopyrans is cyanated; (7) the reaction is compatible with a wide range of functional groups. We believe that this simple and efficient catalytic system would be widely applicable to synthesis of various aryl/heteroaryl nitriles.

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