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Palladium-Catalyzed Cyanation of Aryl Halides using Formamide and Cyanuric Chloride as a New "CN" Source

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Abstract: A new source of "CN" employing formamide and cyanuric chloride is introduced for the cyanation reactions. The treatment of formamide and 2,4,6-trichloro-1,3,5-triazine (TCT; cyanuric chloride) afforded an efficient cyanating agent which it can be used as a nontoxic, readily available and non-expensive reagent in the cyanation transformations. In this study, palladium-catalyzed cyanation of aryl halides was successfully accomplished using this new "CN" source in high yields.

Introduction

Benzonitriles are an important class of organic compounds with a broad applications which serve as raw material in pharmaticual, natural products, advanced materials, dyes and agriculture chemicals (Figure 1).[1]

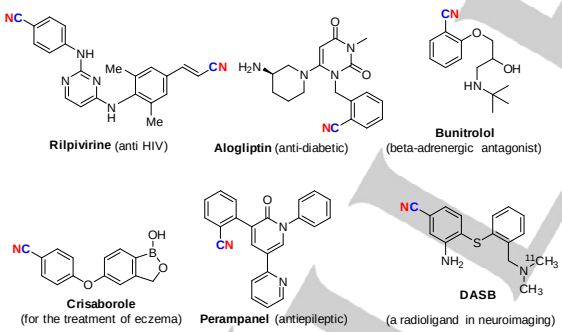
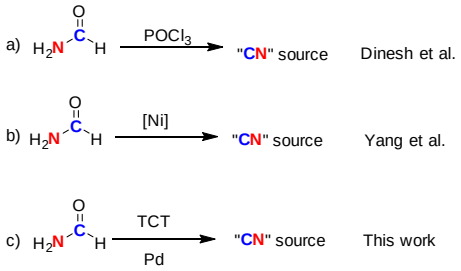


Figure 1. The chemical structure of some biologically important benzonitrile derivatives

These compounds also have been used as valuable precursors for the synthesis of amines, aldehydes, ketones, carboxylic acids, imines and etc.[2] To prepare benzonitrile derivatives, different reactions and methodologies were developed. Sandmeyer reaction, Rosenmund-von Braun reaction, transition metal catalyzed cyanation reactions and C-H bond functionalization of arenes are well-known aryl cyanation methods.[3] In the cyanation reactions, both organic and inorganic cyanide sources have been used. Metal cyanating agents such as NaCN, KCN, CuCN, $K_4Fe(CN)_6$ and $Zn(CN)_2$ are well known in the cyanation reactions. In the case of organic cyanide sources, there are good results with cyanating agents such as cyanohydrin, acetonitrile, malononitrile and benzyl cyanide.[1-3] However, some of the available cyanide sources suffer from some drawbacks to be used in cyanation reactions including high toxicity, low solubility, less reactivity, high sensitivity to moisture, high pricing, and formation of metal wastes in a stoichiometric amount.[4] Due to these limitations, the discovery of new sources of "CN", especially its *in situ* generation from simple and readily available regents, is highly considered in recent years.[5-11] The safety of these combined cyanating reagents has attracted much attention and has made it an important topic in this field.[8a,c,9b] Yu's group reported the use of nitromethane as the cyanide source for the cyanation of 2-phenylpyridine.[5] A combined cyanide source using ammonia and DMF was disclosed for the C-H cyanation of 2-arylpyridine, electron-rich arenes, aryl boron compounds, indoles and organosilanes.[6] DMF was also used as a cyanide source alone.[7] Also, a combination of DMF and NH_4X (X = HCO_3, I) was illustrated for the cyanation of aryl halides.[8] In addition, dimethyl sulfoxide (DMSO) in combination with NH_4HCO_3 was also worked well as CN source for the cyanation of the 3-position of indole.[9a] DMSO in combination with urea in the presence of CuF_2 was used as "CN" source in the cyanation of aryl iodides.[9b]

Formamide in the presence of $POCl_3$ was also produces a cyanide source for the cyanation of aryl halides (Scheme 1, a).[10] Very recently a nickel-catalyzed process was developed using formamide to generate "CN" source for cyanation reactions (Scheme 1, b).[11] In this study we disclosed a new nontoxic cyanide source using combination of formamide and 2,4,6-trichloro-1,3,5-triazine (TCT; cyanuric chloride) (Scheme 1, c). This precursor is an efficient and operationally simple cyano source that it generates cyanuric acid as a byproduct which is simply removable from the reaction mixture.



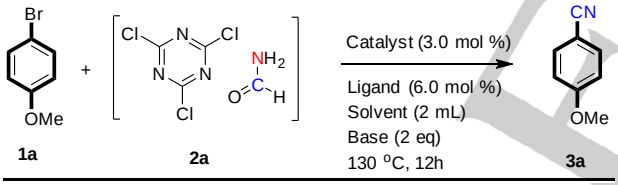
Scheme 1. The use of formamide as "CN" precursor.

In continuation of our program on application of TCT in organic transformations,[12,13] it was found that its combination with formamide produces a stable salt, which it can be used as a safe, easily handling reagent in the cyanation reactions. To the best of our knowledge there is no report in the literature on the use of this reagent in the cyanation reactions. In this study, TCT-formamide salt was used for the cyanation of aryl halides using a Pd-catalyzed process.

Results and Discussion

We investigated the cyanation of 1-bromo-4-methoxybenzene (**1a**) using TCT-formamide reagent (**2a**) in the presence of Pd/C catalyst system as a model reaction (Table 1).

Table 1. Optimization of the reaction conditions [a]



entry	solvent	base	Catalyst (mol %)	Temp(°C)	Yield **3a** (%)[b]
1	DMF	K_2CO_3	Pd/C(3)	130	70
2	$HCONH_2$	K_2CO_3	Pd/C(3)	130	78
3	DMAC	K_2CO_3	Pd/C(3)	130	66
4	Toluene	K_2CO_3	Pd/C(3)	130	30
5	DMSO	K_2CO_3	Pd/C(3)	130	64
6	PEG-300	K_2CO_3	Pd/C(3)	130	55
7	$HCONH_2$	K_2CO_3	Pd/C(3)	130	80[c]
8	$HCONH_2$	K_2CO_3	$Pd(OAc)_2$(3)	130	71[c]
9	$HCONH_2$	K_2CO_3	$PdCl_2$(3)	130	74[c]
10	$HCONH_2$	K_3PO_4	Pd/C(3)	130	62[c]
11	$HCONH_2$	Na_2CO_3	Pd/C(3)	130	78[c]
12	$HCONH_2$	Cs_2CO_3	Pd/C(3)	130	75[c]
13	$HCONH_2$	Et_3N	Pd/C(3)	130	74[c]
14	$HCONH_2$	-	Pd/C(3)	130	40[c]
15	$HCONH_2$	K_2CO_3	Pd/C(3)	130	78[c,d]
16	$HCONH_2$	K_2CO_3	Pd/C(3)	130	52[c,e]
17	$HCONH_2$	K_2CO_3	Pd/C(3.5)	130	84[c,f]
18	$HCONH_2$	K_2CO_3	Pd/C(4.0)	130	83[c]
19	$HCONH_2$	K_2CO_3	Pd/C(3.5)	130	86[c,g]
20	$HCONH_2$	K_2CO_3	Pd/C(3.5)	130	83[c,h]
21	$HCONH_2$	K_2CO_3	Pd/C(3.5)	120	78[c,i]
22	$HCONH_2$	K_2CO_3	Pd/C(3.5)	145	84[c]
23	$HCONH_2$	K_2CO_3	Pd/C(3.5)	130	45[c,i]

[a] Reaction conditions: 4-bromoanisole (1.0 mmol), TCT-formamide salt (0.35 mmol), base (2.0 mmol), catalyst (3.0 mol %), PPh3 (6.0 mol %), and solvent (2.0mL). [b] Isolated yield. [c] TCT was used instead of TCT-formamide salt. [d] 6.0 mol % dppe used as ligand. [e] No ligand was used. [f] 7.0 mol % of PPh_3 used as ligand. [g] 1.5 mmol of base was used. [h] 1mmol base was used. [i] 30 mol% of PPh_3 ligand was used.

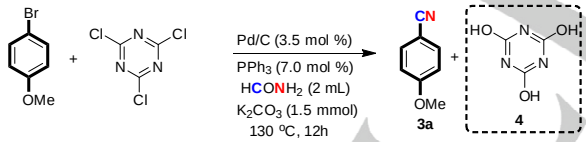
Initially, in DMF solvent in the absence of any direct cyanide source 70% yield of **3a** was produced (Table 1, entry 1). By change of solvent to formamide, the reaction yield was enhanced to 78 % (Table 1, entry 2). Other solvents were also checked and no superiority in the reaction yield was observed, thus formamide was used as solvent for this reaction (Table 1, entries 3-6). By distinguishing formamide as the best solvent for this reaction (among tested solvents) we hypothesized the cyanation reaction using one-pot approach. To our surprise the one-pot procedure (using TCT instead of TCT-formamide salt) worked well and afforded to 80% of isolated product after 12h (Table 1, entry 7). Then, different sources of palladium were used, but no superiority was observed in the reaction yield (Table 1, entries 8 & 9). Therefore, Pd/C as an available and cheap palladium catalyst source was selected for this reaction.[14]

The type of base was also investigated and K_2CO_3 as the best one was distinguished (Table 1, entries 10-14). No change in the reaction yield was observed by the use of 1,2-bis (diphenylphosphino) ethane (dppe) ligand and consequently PPh_3 as readily available ligand was selected (Table 1, entry 15). In the absence of phosphine ligand the reaction yield was decreased to 52 % (Table 1, entry 16). The catalyst loading was evaluated and 3.5 mol% of the catalyst recognized as optimum (Table 1, entries 17 & 18). The amount of base was also checked and result shows that 1.5 mmol of K_2CO_3 was sufficient to obtain high yield (Table 1, entry entries 19 & 20). It seems that, the reaction temperature of higher than 130 °C is essential for the formation of cyanide source from TCT and formamide, so that the reaction yield was decreased at lower temperature (Table 1, entry 21). In addition, at higher temperature of 140 °C, no enhancement in the reaction yield was observed (Table 1, entry 22).

In an experiment in order to show that the reaction is homogeneous or heterogeneous in practice, the amount of PPh_3 was increased to 30 mol% and it was found a remarkable decreasing in the reaction yield (Table 1, entry 23). Since, the PPh_3 ligand can strongly block the active centres of the Pd catalyst, representing a homogeneous Pd-catalyzed cyanation process.

In order to further prove that the "CN" unit is come from formamide component, some other experiments were also accomplished and results are summarized in Scheme 2. In the absence of TCT, no benzonitrile product observed, demonstrating the activation role of TCT to form "CN" source. No product was observed using only TCT or 1,3,5-triazine-2,4,6-triol (**4**; as byproduct of the reaction)[15] confirming that they cannot act as source of "CN", alone. In this light, 2,4,6-triamino-1,3,5-triazine was also checked, possibly it can form "CN" source, but no aryl nitrile product was detected. These experiments confirmed that the "CN" unit is not originated from triazine ring. Based on our experiments, only, using both TCT and formamide components together the cyanation reaction was carried out. The release of cyanide ion was distinguished using picrate impregnated indicator paper upon heating formamide and TCT under optimized reaction conditions. By increasing the amount of TCT to 0.5 equivalents the reaction yield was enhanced to 90%. It is not possible to obtain aryl cyanide using DMF instead of formamide under optimized reaction conditions.[13]

In order to show the formation of cyanide ion using TCT-formamide salt, some NMR experiments was accomplished. In an experiment TCT-formamide was treated with base in DMSO-d_6 solvent and it was heated until 130 °C and it was analyzed by NMR. The ^{13}C NMR show that the peak at 150.0 ppm which is related to the formamide part was completely removed and a peak at 163.1 ppm remained with a little change in chemical shift, corresponding to the triazine ring. This experiment has same results, when in addition to base, Pd source was also used. Also some peaks between 125-130 ppm were observed which can be corresponded to the cyanide ion species. More importantly, no peaks observed in the range of 160 ppm, which is related to the cyanate (-OCN) formation. The generation of cyanate is possible through the oxidation of TCT-formamide reagent, to be served as cyanating agent (see supporting information).[14]

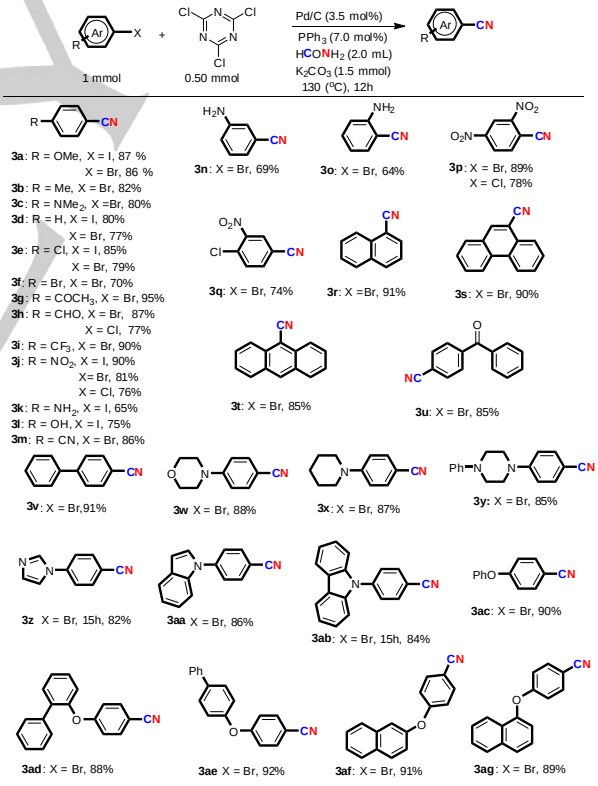


"CN" source	3a (%)[a]	"CN" source	3a (%)[a]
$HCONH_2$	0	TCT (0.35 mmol) + $HCONH_2$	85
TCT (0.5 mmol)	0	TCT (0.5 mmol) + $HCONH_2$	90
1,3,5-triazine-2,4,6-triol (**4**)	0[b]	TCT (0.6 mmol) + $HCONH_2$	90
2,4,6-triamino-1,3,5-triazin	0[c]	TCT (0.5 mmol) + $HCONMe_2$	0[d]

Scheme 2. Control experiments for the cyanation of aryl halides using TCT-formamide as "CN" source. Reaction conditions: 4-bromoanisole (1.0 mmol), TCT (0.35-0.6 mmol), K_2CO_3 (1.5 mmol), Pd/C (3.5 mol %), 7.0 mol % PPh_3, formamide (2.0 mL). [a] Yields corresponds to the isolated products. [b] 0.5 mmol of **4** was used as "CN" source. [c] 0.5 mmol of 2,4,6-triamino-1,3,5-triazin was used as "CN" source. [d] DMF was used as solvent.

With the optimized cyanation conditions in our hand, the substrate scope was investigated (Scheme 3). Cyanation of 1-bromo-4-methoxybenzene and its iodo analog afforded to **3a** in high yields. Then, different bromobenzene and iodobenzene derivatives were tested and high yields of products were obtained. Our results showed that, the type of substituents in viewpoint of the electronic and/or steric difference is not more important factor in the cyanation of aryl halides using TCT-formamide salt. Also, the optimized reaction conditions are compatible with a variety of functional groups such as amine (**3c**,**k**,**n**,**o**,**w**,**x**,**y**), halogens (**3e**,**f**,**q**), keto (**3g,u**), aldehyde (**3h**), nitro (**3j,p,q**), cyano (**3m**) and ether (**3a,ac-ag).** The position of substituents on aromatic ring not have remarkable effects on the reaction yields (**3k,n,o**).

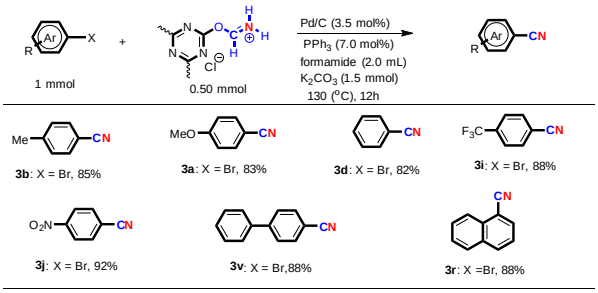
In the case of bihalides the cyanation were selectively accomplished on more active C-halogen bond to afford corresponding halogen-substituted benzonitriles (**3e,f,q**). Polyaromatic aryl halides were easily cyanated using this new "CN" source under optimized conditions without any problem (**3r-t**). Some of the synthetic aryl halides incorporating various heterocycles including morpholine (**3w**), piperidine (**3x**), piperazine (**3y**), imidazole (**3z**), indole (**3aa**), carbazole (**3ab)** were examined in the cyanation reaction and the corresponding nitrile derivatives produced in good to excellent yields. Moreover, bromo-functionalized aryl-aryl ether compounds afforded the aryl-nitrile products (**3ad-ag**). Under optimized reaction conditions aryl chloride derivatives were also checked and moderate to good yields of products were obtained (**3h,j,p**).



Scheme 3. Synthesis of aryl cyanides using TCT and formamide as a combined cyanide source. Reaction conditions: aryl halide (1.0 mmol), TCT (0.5 mmol), K_2CO_3 (1.5 mmol), catalyst (3.5 mol %), PPh_3 (7.0 mol %) and formamide (2.0 mL) at 130 °C. Yield corresponds to isolated products.

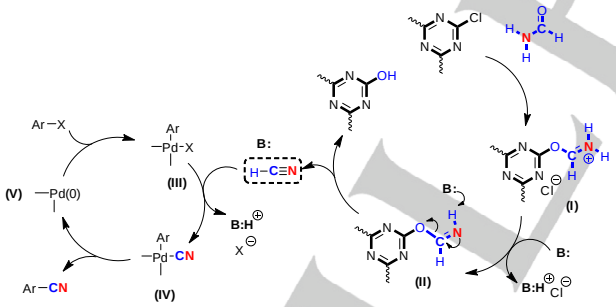
In order to show that TCT-formamide slat is also effective in the cyanation reaction as an alternative for the *in situ* method we

also investigated the cyanation of some aryl halides TCT-formamide slat and results are summarized in Scheme 4. As shown in Scheme 4, the reaction yields are same to the *in situ* method and in some cases the yield is better.



Scheme 4. Synthesis of aryl cyanides using TCT-formamide reagent. Reaction conditions: aryl halide (1.0 mmol), TCT-formamide (0.5 mmol, 0.12 g), K_2CO_3 (1.5 mmol), catalyst (3.5 mol %), PPh_3 (7.0 mol %) and formamide (2.0 mL) at 130 °C. Yields correspond to isolated product.

A plausible reaction mechanism for the cyanation of aryl halides using TCT-formamide reagent was proposed (Scheme 5).[9, 11] The reaction of formamide with TCT forms imminium salt (**I**), which it was isolated and characterized (see supporting information). This salt probably in the presence of a base can form a formimidate intermediate (**II**). The intermediate **II** in the presence of base can release cyanide source, probably through a rearrangement. The oxidative addition of aryl halide to Pd(0) generates a palladated intermediate (**III**). The ligand exchange of CN with halide afforded to Pd(**II**) species (**IV**). Finally, the reductive elimination of intermediate **IV** delivers the cyanation product and regenerates Pd(0).



Scheme 5. Proposed reaction mechanism for the cyanation reaction with TCT-formamide reagent.

Conclusion

In summary, we have introduced a new procedure for the production of a cyano unit from two readily accessible resources including cyanuric chloride and formamide. The cyanation reaction in the presence of this new cyanide source represents an expedient and safe process for the cyanation of the aryl halides. This new developed safe cyanide source may have potential utility in other cyanation reactions.

Experimental Section

General

Chemicals were purchased from Fluka and Aldrich companies and used without further purification. The known products were characterized by comparison of their spectral and physical data with those reported in the literature. ^{1}H (250 MHz), (400MHz), (500 MHz) and ^{13}C NMR (62.5 MHz), (100MHz), (125 MHz) spectra were recorded on a Brucker (250 MHz) Avance DRX and Brucker (400 MHz) Avance DRX in deutrated solvents. FT-IR spectroscopy (Shimadzu FT-IR 8300 spectrophotometer), were employed for characterization of the products. Melting points were determined in open capillary tubes in a Buchi melting point B-545. The reaction monitoring was accomplished by TLC on silica gel PolyGram SILG/UV254 plates. Column chromatography was carried out on columns of silica gel 60 (70−230 mesh).

Synthesis and Characterization of TCT-formamide salt (I). Into two-necked round-bottomed flask (10 mL) equipped with a condenser, TCT (0.18 g, 1.0 mmol), and formamide (4.0 mL) was added and the mixture was stirred for 6h at 100°C. After allowing the mixture to cool down to room temperature, precipitate was filtered and then washed with acetone (3×10 mL). The purified product was dried in an oven at 100 °C for 12 h to afford the TCT-formamide salt **(I)** (0.30 g, 94%) as a brown solid. This compound is soluble in water and DMSO and insoluble in ethyl acetate and acetone.^{1}H NMR (500 MHz, DMSO) δ 11.13 (s, 3H), 7.94 (dd, *J* = 13.5, 1.7 Hz, 1H), 7.64 – 7.04 (m, 5H).^{13}C {^{1}H} NMR (126 MHz, DMSO) δ 163.14, 150.02. IR (KBr) ν: 3402, 3209, 3047, 1720, 1418, 1396, 1056, 779, 540cm^{-1}. It decomposed at above 300 °C. [16]

General procedure for the cyanation of aryl halide using TCT-formamide reagent

Method A: Into two-necked round-bottomed flask (10 mL) equipped with a condenser, aryl halide (1.0 mmol), Pd/C (3.5 mol %, 0.075 g), PPh_3 (7.0 mol %, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5 mmol, 0.2 g), and formamide (2.0 mL) was added and the mixture was stirred for 10 minutes at 25-30°C. Then the resulting mixture was stirred in an oil bath for 12-14 h at 130 °C. After allowing the mixture to cool down to room temperature, water (4.0 mL) was added and then the organic layer extracted with ethyl acetate (3×10 mL).The extracted organic layers were dried over anhydrous Na_2SO_4 and evaporated under vacuum. The crude product was purified by column chromatography, eluting with *n*-hexane/ EtOAc (v/v), to afford the pure product.

Method B: The procedure was same to method **A**, only instead of TCT the TCT-formamide salt (0.5 mmol, 0.12 g) was used.

Spectral data for all synthesized compounds

4-Methoxybenzonitrile (3a). According to the general procedure, a mixture of 4-bromoanisole (1.0 mmol, 0.19 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5 mmol, 0.2g), and formamide (2.0 mL) was stirred at 130 ºC for 12h.The workup process was same tothe general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane /EtOAc20:2 (v/v) to afford the pure compound **3a** (110 mg, 86% yield) as a white solid. ^{1}H NMR (250 MHz, $CDCl_3$):δ 7.57 (d, *J* = 9.0 Hz, 2H), 6.94 (d, *J* = 8.5 Hz, 2H), 3.85 (s, 3H). IR (KBr) ν: 3023, 2977, 2955, 2900, 2841, 2602, 2560, 2218, 1904, 1770, 1606, 1510, 1368, 1361, 1304, 1258, 1176, 1144, 1114, 1023, 958, 829, 808, 715, 682, 645cm^{-1}.The spectral data and physical properties were identical to that previously reported. M.p 53-55 ºC [Lit. 51-53ºC].[17]

4-Methylbenzonitrile (3b). According to the general procedure, a mixture of 4-bromotoluene (1.0 mmol, 0.17 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5mmol,

0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12h. The workup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane/EtOAc 20:1 (v/v) to afford the pure compound **3b** (96 mg, 82% yield).^{1}H NMR (250 MHz, $CDCl_3$): δ7.49 (d, *J* = 8.2 Hz, 2H), 7.23 (d, *J* = 8.2 Hz, 2H), 2.39 (s, 3H, CH_3). IR (KBr) v: 3039, 2877, 2715, 2229, 1921, 1792, 1608, 1508, 1490, 1275, 1177, 1120, 1042, 1022, 951, 817, 761, 706, 605cm^{-1}.The spectral data and physical properties were identical to that previously reported. Colorless oil.[18]

4-(Dimethylamino) benzonitrile (3c). According to the general procedure, a mixture of 4-bromo-*N*,*N*-dimethylaniline (1.0 mmol, 0.20 g), Pd/C (3.5 mol %, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5 mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12h. The workup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane/EtOAc 20:4 (v/v) to afford the pure compound **3c** (117 mg, 80% yield) as a white solid. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.44 (d, *J* = 9.2 Hz, 2H), 6.61 (d, *J* = 9.0 Hz, 2H), 3.02 (s, 6H). IR (KBr) v: 2907, 2869, 2823, 2211, 2159, 1900, 1606, 1557, 1525, 1446, 1417, 1371, 1325, 1226, 1172, 1138, 1122, 1066, 1003, 941, 819, 786, 655, 645, 545cm^{-1}. The spectral data and physical properties were identical to that previously reported. M.p. 71-73 ^{o}C [Lit. 74- 75 ^{o}C].[19]

Benzonitrile (3d). According to the general procedure, a mixture of bromobenzene (1.0 mmol, 0.16 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (2.5 mmol, 0.17 g), and formamide (2.0 mL) was stirred at 130 ºC for 12h. The workup process was same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane to afford the pure compound **3d** (79 mg, 77% yield).^{1}H NMR (250 MHz, $CDCl_3$): δ 7.61-7.66 (m, 2H), 7.56-7.60 (m, 1H), 7.42-7.49 (m, 2H). IR (KBr) v: 3062, 2923, 2229, 1689, 1596, 1488, 1450, 1388, 1288, 1188, 1064, 1026, 925, 840, 756, 686 cm^{-1}. The spectral data and physical properties were identical to that previously reported. Colorless oil.[11]

4-Chlorobenzonitrile (3e). According to the general procedure, a mixture of 1-iodo-4-chlorobenzene (1.0 mmol, 0.24 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12h. The workup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane/EtOAc 20:2 (v/v) to afford compound **3e** (116 mg, 85% yield) as a white solid. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.59 (d, *J* = 8.7 Hz, 2H), 7.45 (d, *J* = 8.7 Hz, 2H). IR (KBr) v: 3085, 2221, 1905, 1643, 1596, 1481, 1396, 1265, 1164, 1087, 825, 702, 586cm^{-1}.The spectral data and physical properties were identical to that previously reported. M.p. 91-93^{o}C [Lit. 90-93^{o}C].[19]

4-Bromobenzonitrile (3f). According to the general procedure, a mixture of 1, 4-dibromobenzene (1.0 mmol, 0.23 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12h. The workup process was same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane /EtOAc 20:2 (v/v) to afford compound **3f** (126 mg, 70% yield) as a white solid. M.p. ^{1}H NMR (250 MHz, $CDCl_3$):δ7.84 (d, *J* = 8.5 Hz, 2H), 7.36 (d, *J* = 8.7Hz, 2H). IR (KBr) v: 2923, 2229, 2160, 1620, 1442, 1265, 1149, 864, 840, 609 cm^{-1}. The spectral data and physical properties were identical to that previously reported. 109-111^{o}C [Lit. 110-113^o C].[20]

4-Acetylbenzonitrile (3g). According to the general procedure, a mixture of 4-bromo acetophenone (1.0 mmol, 0.20 g), pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5 mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12h. The workup process was same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane/EtOAc 20:5 (v/v) to afford compound **3g** (138 mg, 95% yield) as a Light yellow solid.^{1}H NMR (250 MHz, $CDCl_3$):δ 8.04 (d, *J* = 8.7 Hz, 2H), 7.77 (d, *J* = 8.7 Hz, 2H), 2.64 (s, 3H). IR (KBr) v: 3085, 2923, 2854, 2229, 1944, 1689, 1604, 1558, 1404, 1357, 1257, 1110, 1072, 1018, 956, 833, 640, 594 cm^{-1}. The spectral data and physical properties were identical to that previously reported. M.p. 55-57 ^{o}C [Lit. 58-59 ^{o}C].[21]

4-Cyanobenzaldehyde (3h). According to the general procedure, a mixture of 4-bromobenzaldehyde (1.0 mmol, 0.18 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12h. The workup process was same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane/EtOAc 20:3 (v/v) to afford compound **3h** (115 mg, 87% yield) as a white solid. ^{1}H NMR (250 MHz, $CDCl_3$):δ10.08 (s, 1H), 7.98 (d, *J* = 8.5 Hz, 2H), 7.83 (d, *J* = 8.5 Hz, 2H). IR (KBr) v: 3085, 3047, 2862, 2754, 2221, 2167, 1704, 1566, 1442, 1296, 1172, 1010, 833, 740, 617, 547 cm^{-1}. The spectral data and physical properties were identical to that previously reported. M.p. 100-101^{o}C [Lit. 98-99 ^{o}C].[21]

4-(Trifluoromethyl)benzonitrile (3i). According to the general procedure, a mixture of 1-bromo-4-(trifluoromethyl)benzene (1.0 mmol, 0.22 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3(1.5 mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12h.The workup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane/EtOAc 20:2 (v/v) to afford compound **3i** (154 mg, 90% yield) as a light yellow solid.^{1}H NMR (250 MHz, $CDCl_3$):δ7.80 (d, J = 8.5 Hz, 2H), 7.73 (d, J = 8.5 Hz, 2H). IR (KBr) v: 3110, 3089, 3060, 3013, 2237, 1796, 1623, 1416, 1399, 1387, 1323, 1162, 1139, 1108, 1068, 1018, 863, 839, 784, 729, 597, 547cm^{-1}. The spectral data and physical properties were identical to that previously reported. M.p 38-39 ^{o}C [Lit. 36-38 ^{o}C].[19]

4-Nitrobenzonitrile (3j). According to the general procedure, a mixture of 1-bromo-4-nitrobenzene (1.0 mmol, 0.20 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5 mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12h. The workup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane/EtOAc 20:3 (v/v) to afford compound **3j** (130 g, 90% yield) as a yellow solid. ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.35 (d, *J* = 9.0 Hz, 2H), 7.88 (d, *J* = 9.0 Hz, 2H). IR (KBr) v: 3109, 2229, 1805, 1666, 1604, 1527, 1350, 1288, 1249, 1103, 1010, 856, 748, 678 cm^{-1}. The spectral data and physical properties were identical to that previously reported. M.p. 146-148^{o}C [Lit. 148-150^{o}C].[22]

4-Aminobenzonitrile (3k). According to the general procedure, a mixture of 4-bromoaniline (1.0 mmol, 0.17 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5 mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12h. The workup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane e/EtOAc 20:5 (v/v) to afford compound **3k** (77 mg, 65% yield) as a white solid. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.38 (d, *J* = 8.7 Hz, 2H), 6.63 (d, *J* = 8.7 Hz, 2H), 4.21 (s, 2H). IR (KBr) v: 3471, 3371, 3209, 2214, 1627, 1512, 1450, 1311, 1172, 1134, 833, 686, 624, 547 cm^{-1}. The spectral data and physical properties were identical to that previously reported. M.p. 85-87 ^{o}C [Lit. 87- 88 ^{o}C].[23]

4-Hydroxybenzonitrile (3l). According to the general procedure, a mixture of 4-bromophenol (1.0 mmol, 0.17 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5 mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12h. The workup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane /EtOAc 20:5 (v/v) to afford compound **3l** (89 mg, 75% yield) as a white solid. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.55 (d, *J* = 8.7 Hz, 2 H), 6.99 (s, 1H, OH), 6.94 (d, *J* = 8.75Hz, 2 H). IR (KBr) v: 3290, 3079, 2885, 2804, 2662, 2581, 2444, 2233, 1904, 1791, 1613, 1602, 1560, 1540, 1508, 1449, 1439, 1375, 1364, 1326, 1284, 1249, 1222, 1208, 1192, 1105, 836, 819, 701, 668 cm^{-}

[1]. The spectral data and physical properties were identical to that previously reported. M.p. 111-112 °C [Lit. 110-111 °C].[21]

Terephthalonitrile (3m). According to the general procedure, a mixture of 4-bromobenzonitrile (1.0 mmol, 0.18 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5 mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12h. The workup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane /EtOAc 20:2 (v/v) to afford compound**3m (**110 mg, 86% yield) as a white solid. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.79 (s, 4H). IR (KBr) v: 3199, 2230, 1681, 1417, 1290, 1121, 1095, 1016, 956, 862, 774, 675, 563, 544cm^{-1}. The spectral data and physical properties were identical to that previously reported. M.p. 224-226°C [Lit. 225-227 °C].[21]

3-Aminobenzonitrile (3n). According to the general procedure, a mixture of 3-bromoaniline (1.0 mmol, 0.17 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12h. The workup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane /EtOAc 20:5 (v/v) to afford compound **3n** (82 mg, 69% yield) as a pale yellow solid. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.22-7.15 (m, 1H), 6.99-6.95 (m, 1H), 6.87-6.82 (m, 2H), 3.96 (s, 2H). IR (KBr) v: 3400, 3325, 3218, 2234, 1600, 1490, 1476, 1457, 1313, 1295, 1167, 1157, 1068, 993, 976, 932, 895, 863, 788, 685cm^{-1}. The spectral data and physical properties were identical to that previously reported. M.p. 52-54 °C [Lit. 47-48 °C].[21]

2-Aminobenzonitrile (3o). According to the general procedure, a mixture of 2-bromoaniline (1.0 mmol, 0.18 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12h. The workup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane /EtOAc 20:5 (v/v) to afford compound **3o** (76 mg, 64% yield) as a yellow solid. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.31-7.18 (m, 2H), 6.68-6.61 (m, 2H), 4.36 (s, 2H). IR (KBr) v: 3459, 3368, 3079, 3037, 2209, 2158, 1626, 1569, 1456, 1436, 1337, 1312, 1266, 1202, 1155, 1029, 847, 745cm^{-1}. The spectral data and physical properties were identical to that previously reported. M.p. 49-51°C [Lit. 48-50 °C].[23]

2, 4-Dinitrobenzonitrile (3p). According to the general procedure, a mixture of 1-bromo-2, 4-dinitrobenzene (1.0 mmol, 0.25 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5 mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12h. The workup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane /EtOAc 20:5 (v/v) to afford compound **3p** (171 mg, 89% yield) as a yellow to orange solid.^{1}H NMR (250 MHz, $CDCl_3$): δ 8.67 (d, *J* = 5.0 Hz, 1H), 8.18 (dd, J = 10.0 Hz, *J* = 2.0 Hz, 1H), 7.01 (d, *J* = 10.0 Hz, 1H). IR (KBr) v: 3078, 2245, 1612, 1512, 1326, 1211, 1118, 1056, 941, 817, 748, 586 cm^{-1}. The spectral data and physical properties were identical to that previously reported. M.p. 102-104°C [Lit. 104-105°C].[24]

4-Chloro-3-nitrobenzonitrile (3q). According to the general procedure, a mixture of 4-bromo-1-chloro-2-nitrobenzene (1.0 mmol, 0.24 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5 mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12h.Theworkup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane /EtOAc 20:2 (v/v) to afford compound **3q** (135 mg, 74% yield) as a white solid. ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.07- 8.02 (m, 1H) 7.59- 7.54 (m, 1H), 7.02 (d, *J* = 10.0 Hz, 2H). IR (KBr) v: 3093, 2221, 1581, 1535, 1342, 1265, 1188, 1087, 964, 879, 810, 748 cm^{-1}. The spectral data and physical properties were identical to that previously reported. M.p. 99-100°C [Lit. 98-101 °C].[25]

1-Naphthonitrile (3r). According to the general procedure, a mixture of 1-bromonaphtalene (1.0 mmol, 0.21 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12h. The workup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane /EtOAc 20:1 (v/v) to afford compound **3r** (140 mg, 91% yield) as a white solid.^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 (d, *J*= 8.0 Hz,1H), 7.95 (d, *J*= 8.0 Hz,1H), 7.83-7.78 (m,2H), 7.58-7.51 (m, 2H), 7.43-7.39 (m, 1H). IR (KBr) v: 3058, 2222, 1604, 1504, 1396, 1242,801, 772 cm^{-1}. The spectral data and physical properties were identical to that previously reported. M.p. 35-37 °C [Lit. 36-38°C].[26]

Phenanthrene-9-carbonitrile (3s). According to the general procedure, a mixture of 1-bromonaphtalene (1.0 mmol, 0.21 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5 mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12h. The workup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane/EtOAc 20:2(v/v) to afford compound **3s** (183 mg, 90% yield) as a yellow solid. ^{1}H NMR (250 MHz, $CDCl_3$):δ8.73-8.67 (m, 2H), 8.32-8.29 (m, 1H), 8.25 (s, 1H), 7.95- 7.91 (m, 1H), 7.84- 7.80 (m, 1H), 7.79- 7.74 (m, 2H), 7.71-7.65 (m, 1H). IR (KBr) v: 3071, 2219, 1616, 1448 1245, 1219, 950, 916, 744, 718, 620, 510, cm^{-1}. The spectral data and physical properties were identical to that previously reported. M.p. 105-107°C [Lit. 109°C].[22]

Anthracene-9-carbonitrile (3t). According to the general procedure, a mixture of 9-bromoanthracene (1.0 mmol, 0.26 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5 mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12h. The workup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane /EtOAc 20:2(v/v) to afford compound **3t** (172 mg, 85% yield) as a green solid. ^{1}H NMR (400 MHz, $CDCl_3$):δ8.51 (s, 1H), 8.31 (d, J = 8.5 Hz, 2H), 7.97 (d, *J* = 8.5 Hz, 2H), 7.64 (t, *J* = 8.2 Hz, 2H), 7.52 (t, *J* = 7.7 Hz, 2H). IR (KBr) v: 3049, 3032, 2213, 1927, 1684, 1646, 1527, 1339, 1262, 1161, 1008, 954, 898, 855, 846, 780, 759, 730 cm^{-1}. The spectral data and physical properties were identical to that previously reported. M.p. 174-176 °C [Lit. 173-177°C].[27]

4-Benzoylbenzonitrile (3u). According to the general procedure, a mixture of 9-bromobenzophenone (1.0 mmol, 0.26 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5 mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12h. The workup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane/EtOAc 20:5 (v/v) to afford compound **3u** (176 mg, 85% yield) as a light white solid. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.87 (d, *J* = 8.5 Hz, 2H): 7.81- 7.76 (m, 4H), 7.67-7.61 (m, 1H), 7.54-7.48 (m, 2H). IR (KBr) v: 3065, 2229, 1743, 1650, 1550, 1535, 1519, 1458, 1311, 1280, 1110, 933, 856, 794, 694, 594, 586 cm^{-1}. The spectral data and physical properties were identical to that previously reported. M.p. 109-112°C [Lit. 111-113 °C].[19]

[1, 1'-Biphenyl]-4-carbonitrile (3v). According to the general procedure, a mixture of 4-bromo-1, 1'-biphenyl (1.0 mmol, 0.23 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5 mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12h. The workup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane /EtOAc 20:1 (v/v) to afford compound **3v** (163 mg, 91% yield) as a pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ7.74-7.67 (m, 4H), 7.61-7.59 (m, 2H), 7.51-7.47 (m, 2H), 7.45-7.43 (m, 1H). IR (KBr) v: 3029, 2227, 1631, 1596, 1095, 847 cm^{-1}. The spectral data and physical properties were identical to that previously reported. M.p. 83-85°C [Lit. 85-86 °C].[28]

4-Morpholinobenzonitrile (3w). According to the general procedure, a mixture of 4-(4-bromophenyl) morpholine (1.0 mmol, 0.24 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g),

K_2CO_3 (1.5 mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12h. The workup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane /EtOAc 20:3 (v/v) to afford compound **3v** (165 mg, 88% yield) as a yellowish solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, *J* = 12.0 Hz, 2H), 6.85 (d, *J* = 12.0 Hz, 2H), 3.84 (d, *J* = 4.0 Hz, 4H), 3.27 (d, *J* = 4.0 Hz, 4H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 153.5, 133.5, 119.9, 114.1, 100.9, 66.5, 47.3. IR (KBr) v: 3073, 2977, 2831, 2214, 1604, 1519, 1450, 1380, 1242, 1180, 1110, 925, 833 cm^{-1}. The spectral data and physical properties were identical to that previously reported. M.p. 80-82°C [Lit. 77- 78 °C].[29]

4-(Piperidin-1-yl) benzonitrile (3x). According to the general procedure, a mixture of 1-(4-bromophenyl) piperidine (1.0 mmol, 0.24 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5 mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12h. The workup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane /EtOAc 20:2 (v/v) to afford compound **3x** (162 mg, 87% yield) as a pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, *J* = 12.0 Hz, 2H), 6.80 (d, *J* = 12.0 Hz, 2H), 3.30-3.29 (m, 4H), 1.65-1.653 (m, 6H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ153.5, 133.4, 120.4, 114.0, 98.6, 48.3, 25.2, 24.2. IR (KBr) v: 2936, 2854, 2214, 1604, 1512, 1450, 1350, 1249, 1180, 1126, 817 cm^{-1}. The spectral data and physical properties were identical to that previously reported. M.p. 57-59 °C [Lit. 54- 55 °C].[30]

4-(4-phenylpiperazin-1-yl) benzonitrile (3y). According to the general procedure, a mixture of 1-(4-bromophenyl)-4-phenylpiperazine (1.0 mmol, 0.32 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5 mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12h. The workup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane /EtOAc 20:6 (v/v) to afford compound **3y** (224 mg, 85% yield) as a white yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (d, *J*= 9.2 Hz, 2H), 7.33-7.29 (m, 2H), 6.96 (d, *J*= 7.6 Hz, 2H), 6.91 (d, *J*= 7.6 Hz, 2H), 3.49 (t, *J* = 5.6 Hz, 4H), 3.34 (t, *J* = 5.6 Hz, 4H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 153.3, 150.9, 133.56, 129.3, 120.5, 120.0, 116.4, 114.4, 100.6, 49.0, 47.3. IR (KBr) v: 2923, 2831, 2214, 1596, 1512, 1450, 1388, 1342, 1226, 1180, 1087, 941, 763, 694 cm^{-1}. The spectral data and physical properties were identical to that previously reported. M.p. 168-170 °C [Lit. 169-170 °C].[31]

4-(*1H*-imidazol-1-yl)benzonitrile (3z). According to the general procedure, a mixture of 1-(4-bromophenyl)-1H-imidazole (1.0 mmol, 0.22 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5 mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 15h. The workup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane/EtOAc/MeOH 20:4:1 (v/v) to afford compound **3z** (139 mg, 82% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (s, 1H), 7.72 (d, *J* = 8.8 Hz, 2 H), 7.45 (d, *J* = 8.8 Hz, 2H), 7.19-7.18 (m, 2H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 140.5, 135.39, 134.2, 131.6, 121.4, 117.8, 117.6, 112.2. IR (KBr) v: 3124, 2229, 1689, 1604, 1510, 1303, 1265, 1056, 833, 771, 655, 547 cm^{-1}.The spectral data and physical properties were identical to that previously reported. M.p. 148-150 °C [Lit. 151-154 °C].[18]

4-(*1H*-indol-1-yl) benzonitrile (3aa). According to the general procedure, a mixture of 1-(4-bromophenyl)-*1H*-indole (1.0 mmol, 0.27 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5 mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12h. The workup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane /EtOAc 20:1 (v/v) to afford compound **3aa** (187 mg, 86% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$):δ7.81 (d, *J* = 8.4 Hz, 2H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.65-7.60 (m, 3H), 7.34 (d, *J* = 4.0 Hz, 1H), 7.30-7.20 (m, 2H), 6.75 (dd, *J* = 3.6, *J* = 0.8 Hz, 1H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 143.5, 135.2, 133.8, 130.0, 127.1, 123.8, 123.3, 121.6, 121.4, 118.5, 110.4, 109.3, 105.8. IR (KBr) v: 3101, 2221, 1604, 1512, 1458, 1342, 1103, 840,748 cm^{-1}. The spectral data and physical properties were identical to that previously reported. M.p. 94-96 °C [Lit. 94-95°C].[32]

4-(*9H*-carbazol-9-yl) benzonitrile (3ab). According to the general procedure, a mixture of 9-(4-bromophenyl)-*9H*-carbazole (1.0 mmol, 0.32 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5 mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 15 h. The workup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane /EtOAc 20:1 (v/v) to afford compound **3ab** (225 mg, 84% yield) as a pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (d, *J* = 8.0 Hz, 2H), 7.91 (d, *J* = 8.0 Hz, 2H), 7.74 (d, *J* = 7.0 Hz, 2H), 7.47-7.42 (m, 4H), 7.36-7.232 (m, 2H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 142.0, 139.9, 133.9, 127.1, 126.4, 124.0, 121.0, 120.6, 118.4, 110.4, 109.5. IR (KBr) v: 3055, 2221, 1596, 1512, 1450, 1334, 1226, 1172, 1110, 840, 756 cm^{-1}. The spectral data and physical properties were identical to that previously reported. M.p. 174-176°C [Lit. 176-177°C].[33]

4-Phenoxybenzonitrile (3ac). According to the general procedure, a mixture of 1-bromo-4-phenoxybenzene (1.0 mmol, 0.249 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5 mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12 h. The workup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane /EtOAc 20:1 (v/v) to afford compound **3ac** (176 mg, 90% yield) as a white to yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (d, *J* = 8.0 Hz, 2H), 7.45-7.41 (m, 2H), 7.28-7.23 (m, 1H), 7.09 (d, *J* = 8.0 Hz, 2H), 7.02 (d, *J* = 8.0 Hz, 2H). IR (KBr) v: 3054, 2227, 1605, 1590, 1247, 1106, 871, 767 cm^{-1}. The spectral data and physical properties were identical to that previously reported. M.p. 42-44 °C [Lit. 42-43 °C].[28]

4-([1, 1'-Biphenyl]-2-yloxy) benzonitrile (3ad). According to the general procedure, a mixture of 2-(4-bromophenoxy)-1, 1'-biphenyl (1.0 mmol, 0.32 gr), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5 mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12 h. The workup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane /EtOAc 20:0.5 (v/v) to afford compound **3ad** (239 mg, 88% yield) as a pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51-7.47 (m, 3H), 7.44-7.27 (m, 8H), 7.11 (d, *J* = 8.0 Hz, 1H), 6.86 (d, *J* = 8.0 Hz, 2H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 161.6, 151.2, 136.9, 134.8, 133.9, 131.7, 129.2, 129.0, 128.30, 127.6, 126.0, 121.8, 118.9, 117.2, 105.3. IR (KBr) v: 3062, 2221.8, 1604, 1496, 1427, 1249, 1164, 1110, 840, 771, 740, 702 cm^{-1}.The spectral data and physical properties were identical to that previously reported.M.p. 128-130°C.[34]

4-([1, 1'-Biphenyl]-4-yloxy) benzonitrile (3ae). According to the general procedure, a mixture of 4-(4-bromophenoxy)-1, 1'-biphenyl (1.0 mmol, 0.325 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5 mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12 h. The workup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane /EtOAc 20:0.5 (v/v) to afford compound **3ae** (250 mg, 92 % yield) as a pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64-7.62 (m, 4H), 7.59-7.57 (m, 2H), 7.46 (t, *J* = 8.0 Hz, 2H), 7.39-7.35 (m, 1H), 7.14 (d, *J* = 8.80 Hz, 2H), 7.06 (d, *J* = 8.0 Hz, 2H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 161.6, 154.3, 140.1, 138.3, 134.2, 128.9, 127.4, 127.0, 120.6, 119.0, 118.9, 118.0, 105.9. IR (KBr) v: 3047, 2221, 1596, 1481, 1249, 1172, 1110, 1010, 825, 732, 694 cm^{-1}. Anal. Calcd for $C_{19}H_{13}NO$ (271.32): C, 84.11; H, 4.83; N, 5.16; O, 5.90. Found: C, 84.17; H, 4.77; N, 5.23. M.p. 99-102°C.

4-(Naphthalene-2-yloxy) benzonitrile (3af). According to the general procedure, a mixture of 2-(4-bromophenoxy) naphthalene (1.0 mmol, 0.30 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5 mmol, 0.2 g), and formamide (2.0 mL) was

stirred at 130 ºC for 12 h. The workup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane /EtOAc 20:1 (v/v) to afford compound **3af** (223 mg, 91 % yield) as a white to yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, *J* = 8.0 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.56-7.49 (m, 3H), 7.26 (dd, *J* = 8.8, *J* = 2.4 Hz, 1H), 7.09 (d, *J* = 8.8 Hz, 2H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 161.6, 152.4, 134.3, 131.0, 130.5, 127.9, 127.3, 126.9, 125.6, 120.2, 118.8, 1181, 116.7, 106.0. IR (KBr)v: 3055, 2221, 1589, 1504, 1465, 11357, 1247, 1164, 1118, 956, 825, 756 cm^{-1}. The spectral data and physical properties were identical to that previously reported. M.p. 100-102°C [Lit. 103-105 °C].[35]

4-(Naphthalen-1-yloxy) benzonitrile (3ag). According to the general procedure, a mixture of 1-(4-bromophenoxy) naphthalene (1.0 mmol, 0.30 g), Pd/C (3.5 mol%, 0.075 g), PPh_3 (7.0 mol%, 0.018 g), TCT (0.5 mmol, 0.092 g), K_2CO_3 (1.5 mmol, 0.2 g), and formamide (2.0 mL) was stirred at 130 ºC for 12 h. The workup process is same to the general procedure. The crude product was purified by column chromatography, eluting with *n*-hexane /EtOAc 20:1 (v/v) to afford compound **3ag** (219 mg, 89 % yield) as a white to yellow solid.^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96-7.91 (m, 2H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.59 (d, *J* = 8.8 Hz, 2H), 7.53 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.50-7.45 (m, 2H), 7.14 (dd, *J* = 7.2, 0.8 Hz, 1H), 7.01 (d, *J* = 8.8 Hz, 2H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 162.3, 150.4, 135.1, 134.2, 128.1, 126.9, 126.6, 125.8, 125.5, 121.6, 118.8, 117.5, 116.3, 105.8. IR (KBr) v: 3055, 2221.8, 1596, 1496, 1388, 1242, 1164, 1072, 840, 771 cm^{-1}. The spectral data and physical properties were identical to that previously reported. M.p. 125-126 °C.[36]

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Keywords: Cyanuric chloride • Cyanation • Combined "CN" source • Palladium • Aryl Halides

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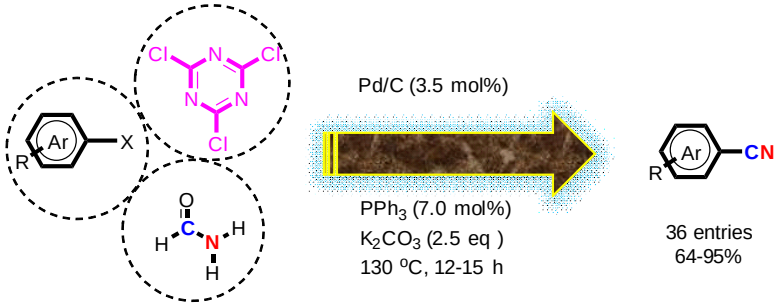

Combination of formamide and cyanuric chloride afforded a new combined “CN” source which is highly stable and safe and can be used in organic cyanation transformation reactions instead of common cyanide sources. This study unfolds the efficient Pd-catalyzed cyanation of aryl halides using TCT-formamide reagent as a new combined “CN” source.