JOC The Journal of Organic Chemistry

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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.7b01332 • Publication Date (Web): 11 Aug 2017

Just Accepted

ACS Publications

The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

Atom – Economic Palladium Carbon Catalysed *de novo* synthesis of Tri- substituted Nicotinonitriles

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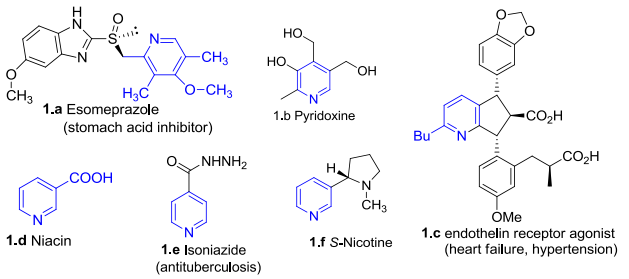
ABSTRACT: A *de novo* Palladium carbon catalyzed synthesis of tri-substituted nicotinonitriles from easily synthesized homopropagylic or homoallylic aromatic alcohols in presence of nitriles has been explored. The mechanism proceeds with an interesting generation of Pd(II) -C palladacycle followed by an oxidative aromatization to generate the pyridine core. The pyridine core is generated with a noteworthy C-C bond cleavage incase with the substituted nitriles. The moderate yields and easy separation of the products delivers a unique importance to this one pot methodology

INTRODUCTION

Aromatic aza-heterocycles play a crucial role in pharmaceuticals, as natural products, functional materials and as well as important reactive intermediates in crucial organic synthesis.[1] Undoubtedly, functionalized pyridines account for the highest range of applications amongst the group of aza-heterocycles. Pyridine analogues play a significant understanding of the chemistry of biological systems. It constitutes the central core of many enzymes like NADP, which involves various oxidation–reduction processes. Vitamins like pyridoxine (1.b) and niacin (1.d) (vitamin B6) constitute another important set. Pyridine analogues comprise of the largest fraction of pharmaceutical drugs (Fig-1). Thus, synthesis of pyridine and its analogues has been a lucrative target throughout years[2]; few of these available approaches are catalytic transformations. The notable reports are $Zn(OTf)_2$-promoted [1+5] cycloaddition of isonitrile with substituted enamides[3], Ag mediated addition of dithianes to unsaturated carbonyls[4] , Rh catalyzed C-H functionalisation of terminal alkynes with ketoximes[5] , Mn mediated reaction of cyclopropanols with vinyl azides[6] and Cu-catalysed oxidative sp^3 C-H coupling.[7] But none of these protocols demonstrate a general atom economic synthetic view point towards these biologically active substituted pyridines. Thus efficient atom-economic catalytic approaches of these functionally engineered pyridines, remains a challenge and enthusiastic task in both academic and industrial scenario. Moreover, approaches engulfing heterogeneous catalysis which do appear as a promising option not only due to easy separation along with scaling up, but also its utility in continuous flow reactors with advantages like wide commercial availability, economic, less heavy metal contamination, has yet to be explored in this direction.



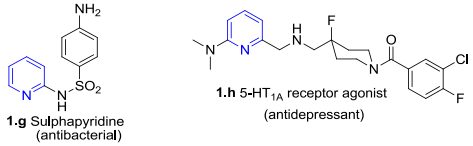
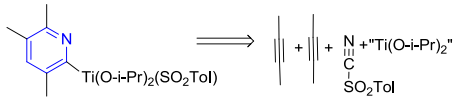


Fig: 1 Biologically active pyridine molecules

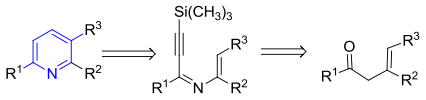
In this connection, it is needless to mention that nicotine derivatives have been one of the most important biologically active members of this group due to their immense use not only as recreational tobacco products but also as their pharmaceutical potency. (*S*)- nicotine has been used as an active drug against many neurodegenerative drugs like Parkinson's , Alzheimer's, Schizophrenia and many other CNS disorders.[8] There have been conscious efforts to synthesize these nicotine derivatives in last decade.[9] The "cyano"-functionality in the pyridyl core can be considered a treasure-well for synthetic transformations. It delivers adequate freedom to a chemist to execute the planned synthetic course. Undoubtedly, substituted nicotinonitriles thus resemble an attractive *aza*-heterocycles, which can be functionalized to the desired pyridine derivatives with ease. Although there has been some interesting non-catalytic approaches, [10] catalytic efforts are scanty on this direction.[11] Interestingly, the mentioned aryl pyridines have also evolved as trustworthy substrates for C-H activation.[12] Thus it appeared to us that an atom-economic, catalytic synthesis of polysubstiuted nicotinonitriles with easily available alkyl nitriles acting as both the nitrogen sources would be a commendable target to achieve. It would be further accomplishing, if the catalyst could be reused delivering a high commercial value. Propargyl and allyl alcohols have emerged as highly effective candidates for metal assisted transformations[13] albeit, to the best of our knowledge, they have not been explored to a satisfactory extent towards synthesis of pyridine derivatives. Palladium catalysts have been well known activator of alkynes.[14] Herein, we report a highly effective atom-economic palladium carbon catalyzed synthesis of trisubstituted 3-cyano-pyridines or "Nicotinonitriles" employing the easily available alkyl nitriles serving as both a solvent and precursors. The heterogenous catalytic system delianates an easy break through to this transformation. The key step involves an unprecedented envisioned palladium assisted domino nucleophilic additions to generate the six membered framework followed by oxidative aromatization with a concomitant C-C bond

cleavage in order to deliver the substituted pyridines in moderate yields and regioselectivity. It is believed that the present strategy outweighs the available classical condensation methodologies like Hantzch synthesis.[15] Reppe's acknowledged syntheses of pyridines proceeding via metallacycle-mediated union of alkynes with nitrile via [2+2+2] cycloadditions (Fig 2 (vii))[16], three component condensation (Fig 3) and the related metallacycle-mediated processes remain substantially limited in scope, suffering from the drawbacks with controlling regioselectivity.[17] We were pleased to discover that this one pot transformation to nicotinonitriles was very generalized and worked well at room temperatures with both homopropargylic and homoallylic alcohol precursors, whereas the latter depicts slightly decreased reaction velocity and yields.

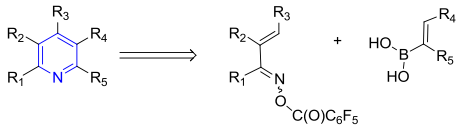
(i) Titanium catalysed metalated pyridines[18]



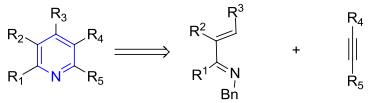
(ii) Ru-catalyzed cycloisomerization[19]



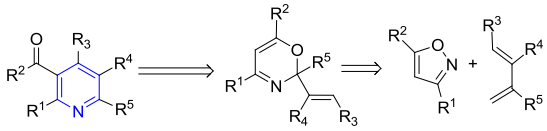
(iii) Cu-catalysed coupling of vinylboronic acids to oxime *o*- carboxylates [20]



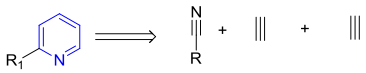
(iv)Rh- catalyzed C-H activation/alkyne insertion.[21]



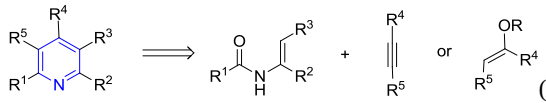
(v) Rh – carbenoid-catalysed ring expansion of isoxazoles[22]



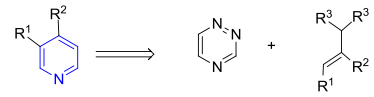
(vi) Electrophilic activation and coupling of vinyl/aryl-amides[23]



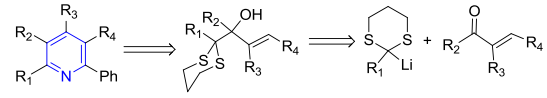
(vii) Metal mediated [2+2+2] cycloaddition[16]



(viii) Cycloaddition[24]



(ix) Ag (I) or Hg (II) –promoted cyclisation[4]



(x) Rhenium catalyzed pyridine synthesis[25]

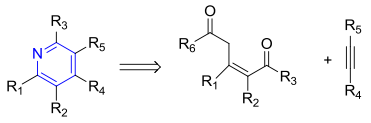


Fig: 2 Synthetic snapshots of substituted Pyridine analogues (Homogenous catalysis)

(i) $K_5CoW_{12}O_{40}.3H_2O$ catalysed 3-component condensation [26]

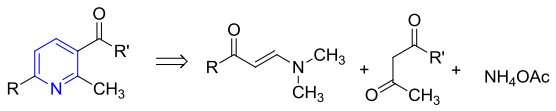
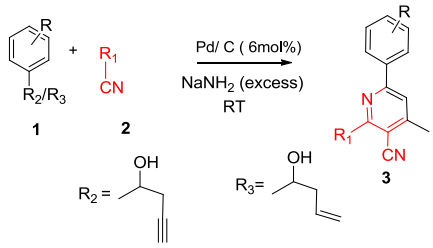


Fig: 3 Synthesis of substituted pyridine analogues (Heterogenous catalysis)

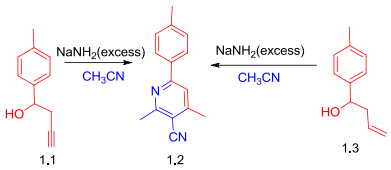
Our work:



RESULTS

We initiated our study by examining the reaction of 1-(p-tolyl)but-3-yn-1-ol (1.1) in acetonitrile as a solvent (Table-1) in presence of a wide variety of heterogenous and homogenous catalytic conditions. In acetonitrile, at ambient temperature, homogenous Pd-catalysts like Pd(dba), $Pd(OAc)_2$ delivered sluggish reaction. Use of other catalysts such as $FeCl_3$, $Co(OAc)_2$, $NiCl_2$, $Cu(OAc)_2$, $CuBr_2$, $Cu(OAc)_2$,$[Cu(CH_3CN)_4]PF_6$, $Ru(CH_3CN)_3PF_6$ catalyzed delivered either no reaction or the oligomerization of isonitrile .While virtually no reaction took place, albeit the catalysts added were more than 20 mol%. Addition of molecular sieves had no effect on the reaction outcome. In a calibrated study in other solvents (Table-1(11-16)), it was concluded that an excess of acetonitrile (20 equivalents) was found necessary for the reaction completion. Use of other bases like KOBu^t, LiHMDS etc (Table-1(17, 18, and 19)) delivered no traces of the product. Under the optimized conditions, the reaction scope was investigated with variety of substrates. (Table.2)

Table-1 Reaction Optimization



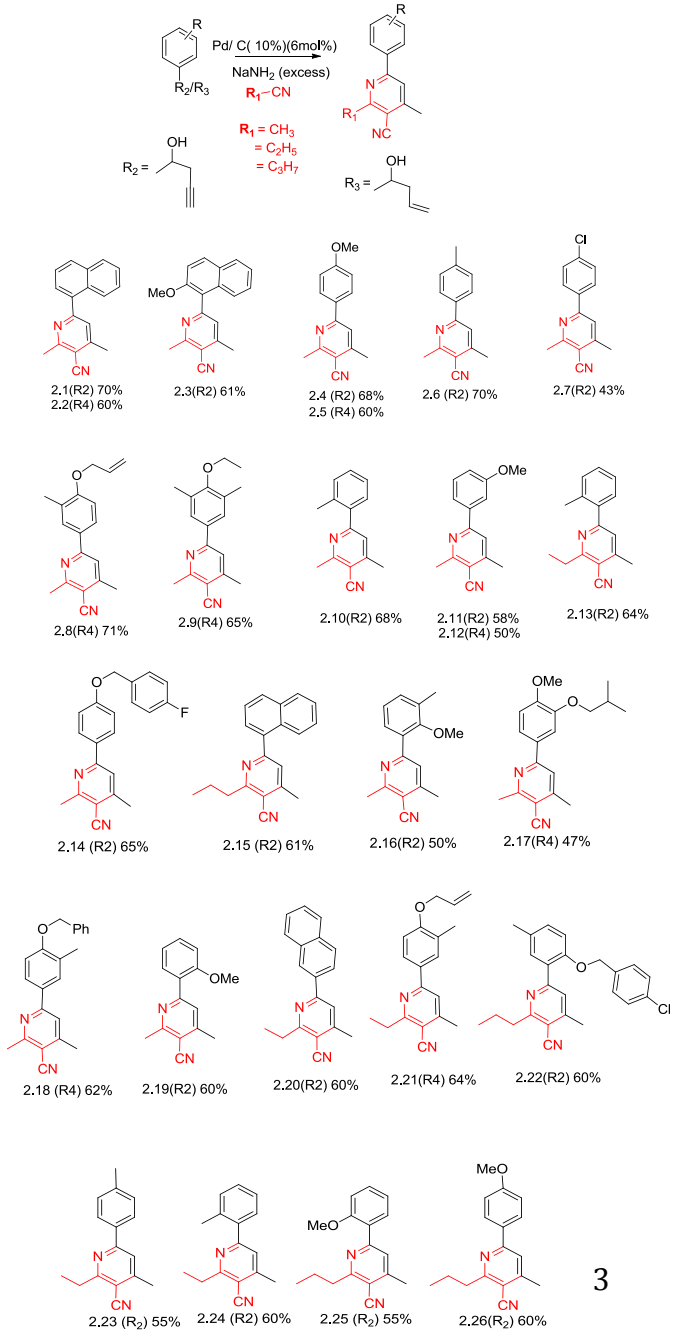
Entry	Catalyst (Mol%)	Base	Solvent	Product (%)	Starting Material Recovered (%)
1	**Pd/C (10%)**	**$NaNH_2$**	CH_3CN	**70**	**10**
2	Pd/C (5%)	$NaNH_2$	CH_3CN	50	20
3	Pd/C (3%)	$NaNH_2$	CH_3CN	23	56
4	Lindlar's catalyst	$NaNH_2$	CH_3CN	5	90
5	Pd 10% (supported on $BaSO_4$)	$NaNH_2$	CH_3CN	56	20
6	$Pd(OH)_2$ on Carbon	$NaNH_2$	CH_3CN	12	70
7	Pd(dba)	$NaNH_2$	CH_3CN	25	60
8	$Pd(OAC)_2$	$NaNH_2$	CH_3CN	28	54
9	$PdCl_2$	$NaNH_2$	CH_3CN	15	72
10	$Pd(PPh_3)_2$	$NaNH_2$	CH_3CN	10	84
11	Pd/C (10%)	$NaNH_2$	Benzene+ CH_3CN (1:1)	30	60
12	Pd/C (10%)	$NaNH_2$	Toluene+ CH_3CN (1:1)	40	50
13	Pd/C (10%)	$NaNH_2$	THF+ CH_3CN (1:1)	15	80
14	Pd/C (10%)	$NaNH_2$	Hexane+ CH_3CN (1:1)	6	90
15	Pd/C (10%)	$NaNH_2$	DMSO+ CH_3CN (1:1)	13	85
16	Pd/C (10%)	$NaNH_2$	DMF+ CH_3CN (1:1)	16	75
17	Pd/C (10%)	n-BuLi	CH_3CN	NR	100
18	Pd/C (10%)	tKOBu	CH_3CN	NR	100
19	Pd/C (10%)	LiHMDS	CH_3CN	NR	100

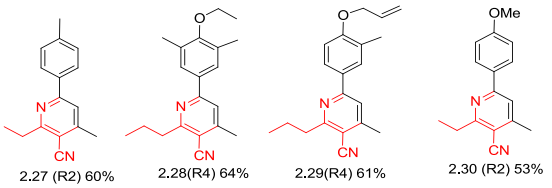
Reaction Conditions: The reaction was conducted with 40mg (0.25 mmol) of 1.1 as substrate, 2.5ml of acetonitrile 195 mg (5 mmol)of $NaNH_2$ and the reaction was tabulated for 10hrs at room temperature (25^0C).The yields specified are obtained after single run.

Excess of the nitrile would be required to drive the reaction to completion. The key oxidative aromatization would deliver the projected trisubstituted nicotinonitrile.

Gratifyingly 1-(*p*-tolyl)but-3-en-1-ol(1.3) on exposure to similar reaction conditions delivered the same nicotinonitrile at room temperature with reduced yields but with longer duration. Increasing the temperature did not accelerate the reaction rate. All of the tested homopropargyl and homoallyl alcohols acted as excellent substrates to react with the nitriles producing the corresponding nicotinonitriles in good to moderate yields. Nevertheless, the reaction was not influenced by the nature of substituent in the phenyl ring but any *ortho*-substitution with respect to the alcoholic moiety significantly retarded the reaction rate presumably due to the steric effects. Running reaction batches in mixture of solvents (Table -1, entries 11-16) with one being the nitrile, exhibited a rapid decrease in the reaction yield highlighting the kinetic molecular encountering playing a dominant role in this transformation and thus rationalize a plausible concerted mechanism involved in the reaction.

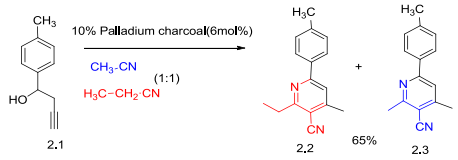
Table-2 Substrate Scope





$PhCH_2CN$ did not react to deliver the substituted pyridines whereas other nitriles like *n*-propionitrile and *n*-butyronitrile delivered better outcomes than acetonitrile. Homopropargyl alcohols acted as marginally better substrates than the corresponding homoallylic alcohols. Thus, it is assumed that the overall rate of the reaction was mainly determined by the steric assignment in the phenyl ring, the substitution pattern in the nitrile as well as the nature of metallic activation of the precursors. The reaction was readily expanded to napthyl homoallylic and homopropargyl alcohols (Table 2(2.1, 2.2)). Halide substitution did not pose any negative effect on the reaction (Table 2 -2.7). The nitriles served as the best solvents to the reaction. The increased challenges associated with such pursuits bear considerations regarding both reactivity and stereo selectivity whereas the current transformation was found to be a worthy demanding process, as running reaction batches in mixture of nitriles delivered two distinct nicotinonitriles in 65 % overall yield (Scheme 1). An assisted C-C bond cleavage is also a part of the process. It is proposed that thermodynamic implausibility related to this unprecedented bond cleavage is compensated by the oxidative aromatization. It also implies, that mixture of two homoallylic alcohols or homopropargyl alcohols or even mixture of either of the homopropagyl alcohol and homoallylic alcohol with the corresponding nitriles delivered only the desired nicotinonitriles in either cases. Thus the issues related to regioselectivity is triumphed over with the advantageous incorporation of the nitriles into the pyridines core in the present study.

Scheme-1 Reaction with bisolvents



To shed light on the involved mechanistic pathway, the reaction was set with a wide range of different homopropargylic substrates enlisted in (Fig-4).

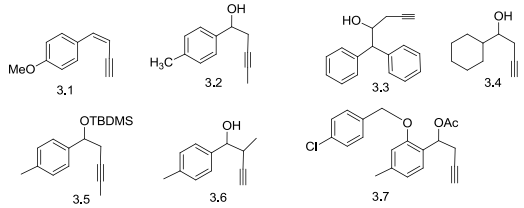
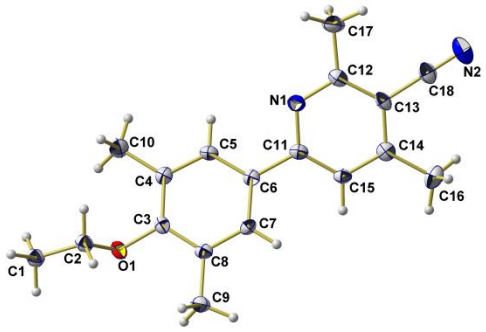


Fig-4 Different substrates tested

No reaction occurred either with substituted alkynes (3.2, 3.4, 3.6), or substituted homoallylic alcohols and alkyl homoallylic alcohols (3.1, 3.5 &3.7).In the ongoing process, an oxidative aromatization[27] induced unprecedented C-C bond cleavage is proposed and the nitrile geometry is insignificant. This finding, that the first alkyl nitrile acts only as a supplier of the nitrile source , plays an important role in the pyridine –forming process and also exhibits profound impact on the potential utility of methodology and provides regiospecific access to a great variety of differentially substituted nicotinonitriles. The charcoal component is expected to stimulate a facile removal of the alkoxy group prompting the desired ring annulations.

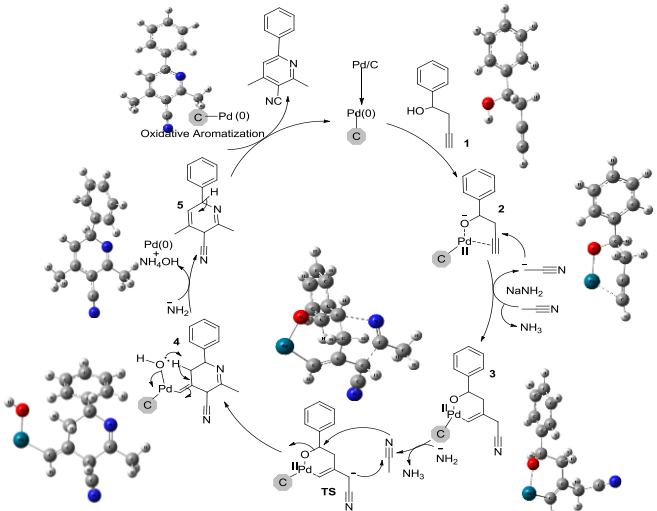
One selected compound (2.9) has been chosen to confirm its composition and to determine its solid state structure (Fig. 5) by single crystal X-ray diffraction.[28] A common feature of this kind of compounds result from the two aromatic rings connected via a slightly shortened C-C single bond [d (C6-C11) = 1.482(3) Å] as steric hindrance will result in their non-coplanarity. Indeed, the dihedral angle between both rings reveals a value of 21.2(1)°, while they are almost planar with all endocyclic bond lengths and angles in the normal ranges.

Fig- 5. Ball-and-stick model and atom numbering scheme of 2.9;



non-hydrogen atoms are drawn as thermal displacement ellipsoids of 50% level. Selected bond lengths (Å) and angles (°): d(C13-C18) = 1.445(3), d(C18-N2) = 1.148(3), <(C13-C18-N2) = 179.8(3), d(C3-O1) = 1.380(2), d(O1-C2) = 1.439(2), d(C1-C2) = 1.494(3), <(C3-O1-C2) = 115.5(1), <(C1-C2-O1) = 107.9(2), d(C4-C10) = 1.505(3), d(C8-C9) = 1.507(3), d(C12-C17) = 1.499(3), d(C14-C16) = 1.495(3).

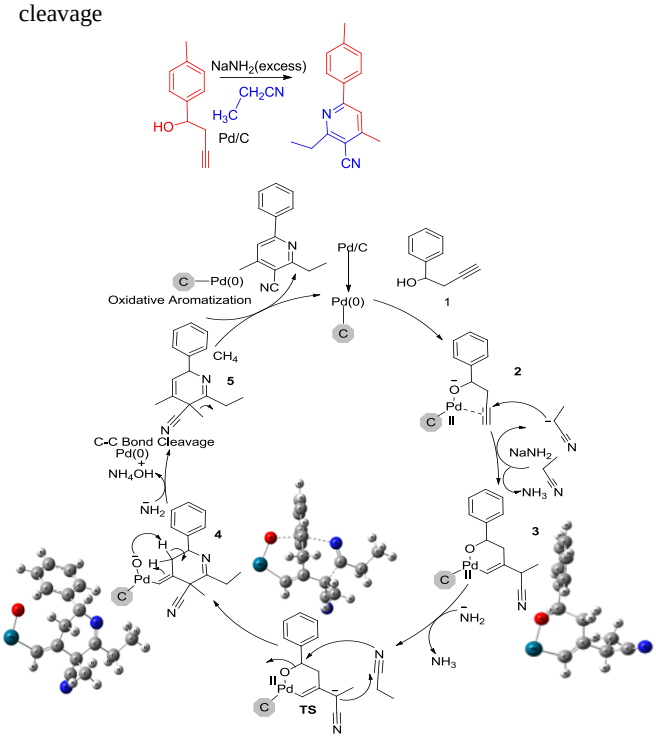
Scheme-2(a) Catalytic cycle with homopropargyl alcohols as primary substrate



The theoretical investigations clearly support the mechanistic outline. The initial step is the formation of the palladacycle (3) (Scheme 2(b)) via oxidative insertion, along with the generation

of charcoal supported Palladium(II). Subsequent base mediated concerted ring annulation and final oxidative aromatization completes the cycle with the regeneration of Pd/C(0). The reaction sequence requires an excess of sodium amide and generates ammonia. There lies a probability of stabilization of solvated electrons in the ammonia generated, which accelerates the oxidative insertion and further accelerates the dearomatization reaction in the catalytic cycle. The formation of the stabilized six membered palladacycle is the driving force for the conversion of Pd(II) from Pd (0). The reaction attains further thermodynamic stability gained through oxidative aromatization. There has been such precedence in heterogenous palladium carbon chemistry.[29] Interestingly, the reaction accelerates with substituted nitriles and encompasses a C-C bond cleavage to deliver the nicotinonitriles. The dignified C-C bond cleavage may be attribute to the aromatic energy gained in the transformation.

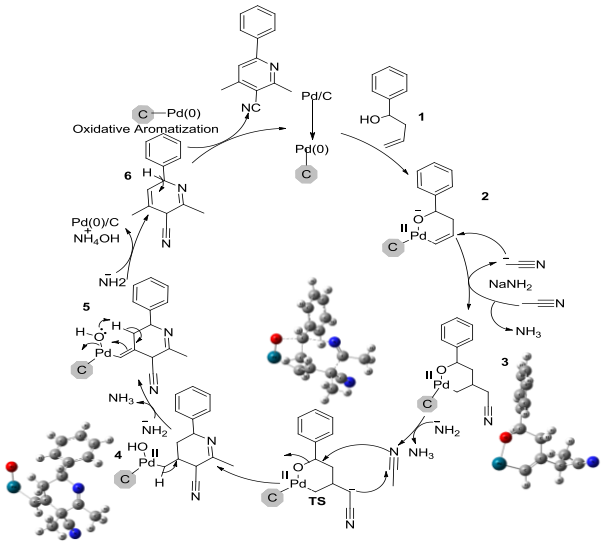
Scheme-2(b) Catalytic cycle with homopropargyl alcohols as primary substrate and substituted nitrile involving C-C bond cleavage



The retarded efficiency of the allylic alcohols in the transformation relates to the slothful tendency of the palladacycle generation in the catalytic cycle, which clearly suported by the theoretical calculation.

The optimized intermediates involved in Scheme 2(a) and (c) are given along with the schemes.The optimization has been performed by using B3LYP form for the generalized gradient approximation (GGA) to the exchange-correlation potential and LANL2DZ form for the basis set embedded in Gaussian09 software.[30] The vibrational frequency calculation has also been performed to make sure that the intermediates are the local minima on the potential energy surface.

Scheme -2(c) Catalytic cycle with homoallylic alcohols as primary substrate



We assumed that the most important phase of the reaction is the formation of six membered ring from 3 to 4. To account that, we have optimized the transition state and calculated the activation energy barrier. The activation energy barrier from 3 to 4 for Schemes 2(a) and Scheme 2(c) are ~13.0 and ~24.0 kcal/mol respectively (Fig. 6). This clearly suggest that why reaction is going faster in homopropargyl alcohol than homoallylic alcohol. We have also checked the same transition state for other substituted nitriles and found that the activation energy barrier is almost comparable (~13.6 kcal/mol) with primary nitrile.

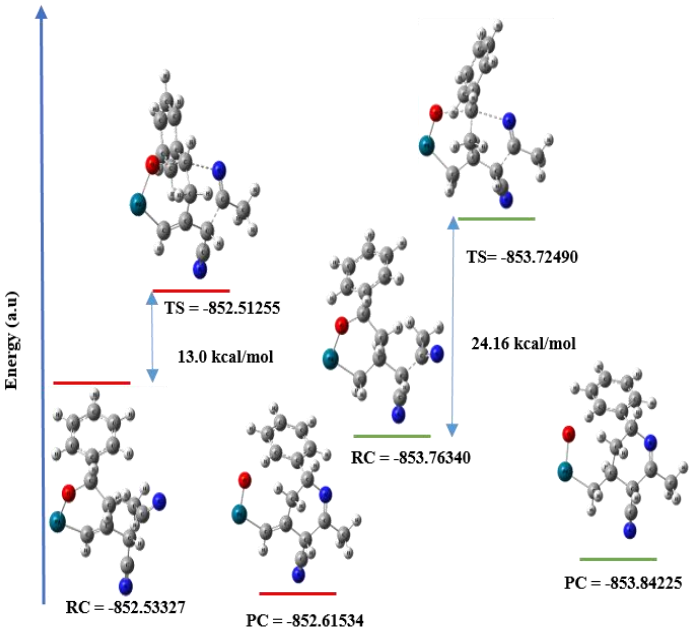


Fig 6: Energy profile diagram from 3 to 4 in Schemes 2(a) and 2 (c). (stands for homopropargyl alcohol with primary nitrile; stands for homoallylic alcohol with primary nitrile; RC = reaction complex; TS = transition state and PC = product complex)

The generated nicotinonitriles can act as facile template for a variety of important transformations towards important molecules like fluorescent indolizine, curindolizine, rosabulin.

CONCLUSION

In conclusion, we have realized an atom-economic synthesis of tri-substituted nicotinoniriles employing cheap nitriles acting both the "N"-sources as well as the solvent of the reaction. The synthesis employs easily available substrates like homo propargyl/allylic alcohol and economic Pd/C catalyst at room temperature. To the best of our information, this is the first synthesis of such trisubstituted nicotinonitriles employing heterogenous catalysis. The sequence leading to the pyridine core encompasses an unprecedented concerted addition of the nitriles to the activated homopropargyl and homoallylic alcohols. The formation of heterogeneous Pd(II)-C followed by the unprecedented oxidative aromatization induced C-C bond cleavage in case of substituted nitriles seems noteworthy and thus rules out any issues with regiospecificity which has been a prime concern in earlier endeavors. The theoretical study distinctly supports the mechanistic outlook. The elite reaction efficiency, good yields ,wide reaction scope, easy availability of starting materials along with products delivers a fast and straight forward route to biologically active tri-substituted nicotionitriles which supersede the available once.

EXPERIMENTAL SECTION

All reactions were carried out under oven dried glassware. Acetonitrile, propionitrile, and butonitrile was dried over potassium carbonate and phoshphorous pentoxide for use. All other reagents were purchased from, Avra chemicals, Sigma-Aldrich, and HIMEDIA and used without further purification. Palladium Charcoal(10%) was purchased from SRL. Na_2SO_4 was dried in oven & used for drying the crude reaction mixture before chromatrography.Chromatography was performed using (100-200mesh) silica gel& neutral aluminium oxide. Analytical TLC was performed with 0.25 mm coated commercial silica gel plates (E.Merck, DC-kiesel gel 60 F_{254}) and visualized with UV light, iodine and vanillin stain. ^1H and ^{13}C NMR spectra were recorded on a Bruker (400 MHz, 100 MHz respectively). Chemical shifts are reported in delta (δ), chemical shift relative to deuterochloroform (7.28 ppm) for ^1H NMR & 77.0 for ^{13}C NMR). Data for ^1H reported as follows- Chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicity recorded as follows s = singlet, d = doublet, t = triplet, q = quartet, m = multiplate, dd = doublet of a doublet. IR spectra were examined by using of a perkin Elmer spectrum-2 spectrometer using Thin film deposit on NaCl plated and frequency reported in absorption (cm^{-1}). High Resolution Mass Spectra (HRMS) were measured in a QTOF I (quadrupole-hexapole-TOF) mass spectrometer with an orthogonal Z-spray-electrospray interface on Micro (YA-263) mass spectrometer

General Procedure for synthesis of Homopropargylic alcohol(A).Aldehyde (1 eq), zinc (1.5 eq) was dissolved in dry THF. The mixture was allowed to stir for 10min then propagyl bromide (1.5 eq) was added. The reaction mixture was stirred for 5hrs. The reaction was then quenched with aqueous solution of ammonium chloride. The organic layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under vaccume. The mass was subjected to column chromatography to afford corresponding homopropargylic alcohol.

General Procedure for synthesis of Homoallylic alcohol(B). Activated magnesium (2eq) (under Iodine) was taken in dry THF. Allyl bromide (1.5eq) was added to the solution and stirred for 15min (until the formation of Grignard reagent),If the Grignard does not form then the mixture was heated with hot water. The aldehyde (1 eq) was added dropwise to the reaction mixture , after completion the reaction mixture was quenched with ammonium chloride solution. The organic layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under vaccume. The mass was subjected to column chromatography over silica gel to afford corresponding homoallylic alcohol.

General Experimental procedure for the synthesis of substituted pyridines(c) . Palladium Charcoal (10%) (6mol%) was added to a well stirred solution of homopropargylic/ homoallyic alcohols in corresponding nitrile (acetonitrile/propionitrile /butonitrile) and stirred for 5mins. Sodium amide (20 eq.) was added to the mixture then the reaction was left for stirring about 10-12h at room temperature. The completion of the reaction was monitored by TLC. After completion of reaction the reaction was quenched with distilled water. The organic layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under vaccume. The mass was subjected to column chromatography over neutral alumina, elution with appropriate solvents afforded corresponding nicotinonitrile.

2, 4-dimethyl-6-(naphthalen-1-yl) nicotinonitrile (2.1) Palladium charcoal (10%)(6 mol%) was added to the well stirred solution of 1-(naphthalen-1-yl)but-3-yn-1-ol(47mg, 0.24mmol) in acetonitrile(5ml). After 5min $NaNH_2$ (195mg, 5mmol) was added to the solution then the reaction mixture allowed to stirred for 9hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with petroleum ether afforded 2, 4-dimethyl-6-(naphthalen-1-yl) nicotinonitrile (2.1) as a white solid (44mg, 70 %) R_f = 0.7 (in 10 % ethyl acetate in petroleum ether). mp 120-125˚C; **^{1}H NMR**(400 MHz, $CDCl_3$); δ = 8.03 (dd, *J* = 7.2Hz, 3.2Hz, 1H), 8.00-7.92 (m, 2H), 7.61-7.511 (m, 4H), 7.39 (s, 1H), 2.89 (s, 3H), 2.63 (s, 3H) **^{13}C NMR** (100 MHz,$CDCl_3$) δ = 161.5, 161.2, 151.4, 136.9, 133.8, 130.6, ,129.7, 128.4, 127.5, 126.7, 126.0, 125.1, 125.0, 123.2, 116.4, 108.1, 23.9, 20.5 , **IR** (Neat Film, NaCl) 2922, 2220, 1587, 1258, 1029, 842 cm^{-1}; **HRMS** (ESI-TOF) m/z: [M + H]+ Calcd for $C_{18}H_{15}N_2$ 259.1235; Found 259.1223.

2, 4-dimethyl-6-(naphthalen-1-yl) nicotinonitrile (2.2) Palladium charcoal (10%)(6mol%) was added to the well stirred solution of 1-(naphthalen-1-yl)but-3-en-1-ol (40mg, 0.20mmol) in acetonitrile(4ml). After 5min $NaNH_2$ (156mg, 4mmol) was added to the solution then the reaction mixture allowed to stirred for 12hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with petroleum ether afforded 2 , 4-dimethyl-6-(naphthalen-1-yl) nicotinonitrile (2.2) as a white solid (31mg, 60 %). Spectra same as 2.1

6-(2-methoxynaphthalen-1-yl)dimethylnicotinonitrile (2.3) Palladium charcoal (10%)(6mol%) was added to the well stirred solution of 1-(2-methoxynaphthalen-1-yl)but-3-yn-1-ol (70mg,.31mmol) in acetonitrile(7ml).After 5min $NaNH_2$ (241mg,6.2mmol) was added to the solution then the reaction mixture allowed to stirred for 12hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with petroleum ether afforded as 6-(2-methoxynaphthalen-1-yl)nicotinonitrile (2.3) a white solid (55mg, 61 %) R_f = 0.6 in 10 % ethyl acetate in petroleum ether. mp 140-145˚C; **^{1}H NMR**(400 MHz, $CDCl_3$); 7.95 (d,

J = 9.2Hz, 1H), 7.85-7.82 (m, 1H), 7.39-7.33 (m, 4H), 7.27 (s, 1H), 3.88 (s, 3H), 2.87 (s, 3H), 2.63 (s, 3H) **^{13}C NMR** (100 MHz, $CDCl_3$) δ =161.5, 158.6, 153.9, 151.0, 132.5, 130.7, 128.8, 127.9, 126.9, 125.0, 124.1, 123.7, 122.3, 116.5, 113.1, 108.2, 56.4, 23.9, 20.4 ; **IR** (Neat Film, NaCl) 2932, 2240, 1580, 1248, 1039, 890 cm^{-1} ; **HRMS**(ESI-TOF) m/z: [M + H]+ calcd for $C_{19}H_{17}N_2O$ 289.1341 ; Found 289.1332.

6-(4-methoxyphenyl)-2, 4-dimethylnicotinonitrile (2.4) Palladium charcoal (10%)(6mol%) was added to the well stirred solution of 1-(4-methoxyphenyl)but-3-yn-1-ol (49mg,.28mmol) in acetonitrile(5ml).After 5min $NaNH_2$ (218mg,5.6mmol) was added to the solution then the reaction mixture allowed to stirred for 8hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with petroleum ether afforded 6-(4-methoxyphenyl)-2, 4-dimethylnicotinonitrile (2.4) as a white solid (45mg, 68 %) R_f = 0.7 in 10 % ethyl acetate in petroleum ether.**^{1}H NMR**(400 MHz, $CDCl_3$); 8.01 (dd, *J* = 6.8Hz, 2Hz, 2H), 7.45 (s, 1H), 7.01 (dd, *J* = 7Hz, 2.4Hz, 2H), 3.89 (s, 3H), 2.81 (s, 3H), 2.57 (s, 3H) **^{13}C NMR** (100 MHz,$CDCl_3$) δ = 161.6, 161.3, 158.5, 151.4, 130.3, 128.8, 117.6, 116.9, 114.2, 107.0, 55.4, 24.0, 20.6; **IR** (Neat Film, NaCl) 2921, 2218, 1583, 1459, 823 cm^{-1} ; **HRMS** (ESI-TOF) m/z: [M + H]+ Calcd for for $C_{15}H_{15}N_2O$ 239.1184; Found 239.1179.

6-(4-methoxyphenyl)-2, 4-dimethylnicotinonitrile (2.5) Palladium Charcoal (10%)(6mol%) was added to the well stirred solution of 1-(4-methoxyphenyl)but-3-en-1-ol (45mg,.25mmol) in acetonitrile(4ml).After 5min $NaNH_2$ (195mg,5mmol) was added to the solution then the reaction mixture allowed to stirred for 12hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with petroleum ether afforded 6-(4-methoxyphenyl)-2, 4-dimethylnicotinonitrile (2.5) as a white solid (36mg, 60 %) R_f = 0.7 in 10 % ethyl acetate in petroleum ether. Spectra same as 2.4

2, 4-dimethyl-6-(p-tolyl)nicotinonitrile (2.6) Palladium charcoal (10%)(6mol%) was added to the well stirred solution of 1-(p-tolyl)but-3-yn-1-ol (80mg,.5mmol) in acetonitrile (8ml).After 5min $NaNH_2$ (390mg, 10mmol) was added to the solution then the reaction mixture allowed to stirred for 7hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with petroleum ether afforded 2, 4-dimethyl-6-(p-tolyl)nicotinonitrile (2.6) as a white solid (79mg, 70 %) R_f = 0.7 in 10 % ethyl acetate in petroleum ether. **^{1}H NMR**(400 MHz, $CDCl_3$); 7.94 (d, *J* = 8Hz, 2H), 7.49 (s, 1H), 7.30 (d, *J* = 8Hz, 2H), 2.82 (s, 3H), 2.58 (s, 3H), 2.43 (s, 3H) **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 161.5, 158.8, 151.4, 140.3, 134.9, 129.5, 127.1, 118.0, 116.6, 107.4, 23.9, 21.2, 20.5; **IR** (Neat Film, NaCl) 2935, 2210, 1510, 1250, 825 cm^{-1} ; **HRMS** (ESI-TOF) m/z: [M + H]+ Calcd for $C_{15}H_{15}N_2$ 223.1235; Found 223.1226.

6-(4-chlorophenyl)-2, 4-dimethylnicotinonitrile (2.7) Palladium Charcoal (10%)(6mol%) was added to the well stirred solution of 1-(4-chlorophenyl)but-3-yn-1-ol (51mg,.28mmol) in acetonitrile (5ml).After 5min $NaNH_2$ (218mg, 5.6mmol) was added to the solution then the reaction mixture allowed to stirred for 12hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with petroleum ether afforded 6-(4-chlorophenyl)-2, 4-dimethylnicotinonitrile (2.7) as a white solid (29mg, 43 %) R_f = 0.7 in 10 % ethyl acetate in petroleum ether. mp 115-120°C; **^{1}H NMR**(400 MHz, $CDCl_3$); 7.99 (dd , *J* = 6.8Hz, 2Hz, 2H), 7.50-7.46 (m, 3H), 2.82(s, 3H), 2.60 (s, 3H); **^{13}C NMR** (100 MHz,$CDCl_3$) δ = 161.7, 157.5, 151.8, 136.2, 136.0, 129.1, 128.9, 118.2, 116.4, 108.1, 23.9, 20.6; **IR** (Neat Film, NaCl) 2933, 2216, 1521, 1240, 815 cm^{-1} ; **HRMS** (ESI-TOF) m/z: [M + H]+ Calcd for $C_{14}H_{12}ClN_2$ 243.0689; Found 243.0673.

6-(4-(allyloxy)-3-methylphenyl)-2,4-dimethylnicotinonitrile (2.8) Palladium Charcoal (10%) (6mol%) was added to the well stirred solution of 1-(4-(allyloxy)-3-methylphenyl)but-3-en-1-ol (30mg, .14mmol) in acetonitrile (3ml).After 5min $NaNH_2$ (109mg, 2.8mmol) was added to the solution then the reaction mixture allowed to stirred for 9hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with petroleum ether afforded 6-(4-(allyloxy)-3-methylphenyl)-2, 4-dimethylnicotinonitrile (2.8) as a white solid (28mg, 71 %) R_f = 0.6 in 10 % ethyl acetate in petroleum ether **^{1}H NMR**(400 MHz, $CDCl_3$); 7.86-7.82 (m, 2H), 7.44 (s, 1H), 6.9 (d, *J* = 8.4Hz, 1H), 6.14-6.05 (m, 1H), 5.49-5.43 (m, 1H), 5.33-5.30 (m, 1H), 4.63-4.622 (m, 2H), 2.80 (s, 3H), 2.56 (s, 3H), 2.34(s, 3H) **^{13}C NMR** (100 MHz,$CDCl_3$) δ =161.4, 158.7, 158.5, 151.2, 133.0, 129.8, 129.6, 127.3, 126.1, 117.5, 117.1, 116.7, 111.1, 106.8, 68.6, 23.9, 20.5, 16.3; **IR** (Neat Film, NaCl) 2905, 2242, 1515, 1220, 827 cm^{-1} ; **HRMS**(ESI-TOF) m/z: [M + H]+ Calcd for $C_{18}H_{19}N_2O$ 279.1497; Found 279.1482.

6-(4-ethoxy-3, 5-dimethylphenyl)-2, 4-dimethylnicotinonitrile (2.9) Palladium Charcoal (10%) (6mol%) was added to the well stirred solution of 1-(4-ethoxy-3,5-dimethylphenyl)but-3-en-1-ol (50mg, .23mmol) in acetonitrile (5ml). After 5min $NaNH_2$ (179mg, 4.6mmol) was added to the solution then the reaction mixture allowed to stirred for 12hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with petroleum ether afforded 6-(4-ethoxy-3, 5-dimethylphenyl)-2, 4-dimethylnicotinonitrile (2.9) as a white solid (44mg, 65 %) R_f = 0.5 in 10 % ethyl acetate in petroleum ether. mp 125-130°C; **^{1}H NMR**(400 MHz, $CDCl_3$); 7.68 (s, 2H), 7.45 (s, 1H), 3.92-3.87 (q, *J* = 7.2Hz, 2H), 2.81 (s, 3H), 2.57 (s, 3H), 2.36 (s, 6H), 1.45 (t, *J* = 6.8Hz, 3H) **^{13}C NMR** (100 MHz,$CDCl_3$) δ = 161.4, 158.8, 157.9, 151.3, 133.0, 131.5, 127.8, 118.1, 116.7, 107.2, 67.9, 23.9, 20.5, 16.4, 15.6; **IR** (Neat Film, NaCl) 2915, 2219, 1535, 1032, 790 cm^{-1} ; **HRMS** (ESI-TOF) m/z: [M + H]+ Calcd for $C_{18}H_{21}N_2O$ 281.1654; Found 281.1648.

2,4-dimethyl-6-(o-tolyl)nicotinonitrile(2.10) Palladium Charcoal (10%) (6mol%) was added to the well stirred solution of 1-(o-tolyl)but-3-yn-1-ol (90mg, .56mmol) in acetonitrile (6ml).After 5min $NaNH_2$ (437mg, 11.2mmol) was added to the solution then the reaction mixture allowed to stirred for4hr. If the reaction does not proceed then reaction mixture was refluxed. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with petroleum ether afforded 2, 4-dimethyl-6-(o-tolyl) nicotinonitrile (2.10) as a white solid (85mg, 68 %) R_f = 0.8 in 10 % ethyl acetate in petro-

leum ether . mp 97-105˚C;**^{1}H NMR**(400 MHz, $CDCl_3$); 7.38-7.27 (m, 5H), 2.83 (s, 3H), 2.60 (s, 3H), 2.37 (s, 3H), **^{13}C NMR** (100 MHz,$CDCl_3$) δ = 162.0, 161.1, 151.2, 138.9, 135.7, 130.9, 129.3, 128.9, 125.9, 122.2, 116.4, 107.7, 23.8, 20.4, 20.2; **IR** (Neat Film, NaCl) 2930, 2214, 1580, 1220, 821 cm^{-1} ;**HRMS** (ESI-TOF) m/z: [M + H]+ Calcd for $C_{15}H_{15}N_2$: 223.1235; Found 223.1229.

6-(3-methoxyphenyl)-2, 4-dimethylnicotinonitrile (2.11)

Palladium Charcoal (10%) (6mol%) was added to the well stirred solution of 1-(3-methoxyphenyl)but-3-yn-1-ol (60mg,.34mmol) in acetonitrile(4ml).After 5min $NaNH_2$ (265mg, 6.8mmol) was added to the solution then the reaction mixture allowed to stirred for 8hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with petroleum ether afforded 6-(3-methoxyphenyl)-2, 4-dimethylnicotinonitrile (2.11) as a colourless liquid (47mg, 58%) R_f = 0.7 in 10 % ethyl acetate in petroleum ether **^{1}H NMR**(400 MHz, $CDCl_3$); 7.62-7.56 (m, 2H), 7.51 (s, 1H), 7.41 (t, *J* = 8Hz, 1H), 7.04-7.01 (m, 1H), 3.91 (s, 3H), 2.84 (s, 3H), 2.60 (s, 3H) **^{13}C NMR** (100 MHz,$CDCl_3$) δ = 163.1, 161.5, 160.2, 153.1, 140.7, 131.3, 121.1, 120.1, 118.0, 117.3, 114.1, 109.5, 56.8, 25.4, 22.1; **IR** (Neat Film, NaCl) 2924, 2215, 1527, 1029, 822 cm^{-1} ; **HRMS** (ESI-TOF) m/z: [M + H]+ Calcd for $C_{15}H_{15}N_2O$ 239.1184; Found 239.1177.

6-(3-methoxyphenyl)-2, 4-dimethylnicotinonitrile (2.12)

Palladium Charcoal (10%) (6mol%) was added to the well stirred solution of 1-(3-methoxyphenyl)but-3-en-1-ol (54mg,.3mmol) in acetonitrile (5ml).After 5min $NaNH_2$ (234mg, 6mmol) was added to the solution then the reaction mixture allowed to stirred for 12hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with petroleum ether afforded 6-(3-methoxyphenyl)-2, 4-dimethylnicotinonitrile (2.12) as a colourless liquid (36mg, 50%) R_f = 0.7 in 10 % ethyl acetate in petroleum ether**.** Spectra same as 2.11

2-ethyl-4-methyl-6-(o-tolyl) nicotinonitrile (2.13) Palladium Charcoal (10%) (6mol%) was added to the well stirred solution of 1-(o-tolyl)but-3-yn-1-ol (40mg,.25mmol) in acetonitrile(4ml).After 5min $NaNH_2$ (195mg, 5mmol) was added to the solution then the reaction mixture allowed to stirred for 6hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with 5% ethyl acetate petroleum ether afforded 2-ethyl-4-methyl-6-(o-tolyl)nicotinonitrile (2.13) as a yellow liquid (38mg, 64 %) R_f = 0.5 in 10 % ethyl acetate in petroleum ether **^{1}H NMR**(400 MHz, $CDCl_3$); 7.41 (d, *J* = 6.8Hz, 1H), 7.34-7.28 (m, 3H including $CDCl_3$), 7.10 (s, 1H) ,3.02 (q, *J* = 7.6Hz, 2H), 2.57 (s, 3H), 2.43 (s, 3H), 1.41 (t, *J* = 7.8Hz, 3H) **^{13}C NMR** (100 MHz,$CDCl_3$) δ =171.4, 167.0, 166.7, 138.2, 135.9, 130.9, 129.2, 129.0, 125.9, 117.3, 32.7, 24.2, 20.2, 12.9; **IR** (Neat Film, NaCl) 2986, 2215, 1577, 894 cm^{-1}; **HRMS** (ESI-TOF) m/z: [M + H]+ Calcd for $C_{16}H_{17}N_2$ 237.1392; Found 237.1386.

6-(4-((4-fluorobenzyl)oxy)phenyl)-2,4-dimethylnicotinonitrile (2.14) Palladium Charcoal (10%) (6mol%) was added to the well stirred solution of 1-(4-((4-fluorobenzyl)oxy)phenyl)but-3-en-1-ol (70mg, .26mmol) in acetonitrile (4ml).After 5min $NaNH_2$ (195mg, 5.2mmol) was added to the solution then the reaction mixture allowed to stirred for 12hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with 5% ethyl acetate petroleum ether afforded 6-(4-((4-fluorobenzyl)oxy)phenyl)-2,4-dimethylnicotinonitrile (2.14) as a white solid (55mg, 65%) R_f = 0.7 in 10 % ethyl acetate in petroleum ether **^{1}H NMR**(400 MHz, $CDCl_3$); 8.01(d, *J* = 8.8Hz, 2H), 7.46-7.42 (m, 3H), 7.12-7.06 (m, 4H), 5.11 (s, 2H), 2.81 (s, 3H), 2.58 (s, 3H) **^{13}C NMR** (100 MHz,$CDCl_3$) δ = 161.5, 160.2, 151.4, 130.6, 129.2, 129.2, 128.7, 117.5, 116.7, 115.5, 115.3, 115.0, 107.0, 69.3, 23.9, 20.5; **IR** (Neat Film, NaCl) 2966, 2218, 1585, 1245, 820 cm^{-1}; **HRMS** (ESI-TOF) m/z: [M + H]+ Calcd for $C_{21}H_{18}FN_2O$ 333.1403; Found 333.1401.

2-methyl-6-(naphthalen-1-yl)-4-propylnicotinonitrile (2.15)

Palladium Charcoal (10%) (6mol%) was added to the well stirred solution of 1-(naphthalen-1-yl)but-3-yn-1-ol (60mg, 0.31 mmol) in butonitrile (6ml).After 5min $NaNH_2$ (234mg, 6mmol) was added to the solution then the reaction mixture allowed to stirred for 6hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with 5% ethyl acetate petroleum ethe afforded 2-methyl-6-(naphthalen-1-yl)-4-propylnicotinonitrile (2.15) as a yellow liquid (53mg, 61 %) R_f = 0.7 in 10 % ethyl acetate in petroleum ether ^{1}H**NMR**(400 MHz, $CDCl_3$); 8.153-8.12 (m, 1H), 7.96-7.91 (m, 2H), 7.64-7.51 (m, 2H), 3.05-3.01 (m, 2H), 2.6 (s, 3H), 1.98-1.93 (m, 2H), 1.07 (t, *J* = 7.6 Hz,3H) **^{13}C NMR** (100 MHz,$CDCl_3$) δ = 170.9 , 166.9, 166.2, 136.3, 133.8, 130.5, 129.7, 128.3, 127.4, 126.6, 125.9, 125.1, 118.4, 41.6, 24.2, 22.4, 13.9; **IR** (Neat Film, NaCl) 2922, 2216, 1588, 1230, 950 cm^{-1}; **HRMS** (ESI-TOF) m/z: [M + H]+ Calcd for $C_{20}H_{19}N_2$ 287.1548; Found 287.1541.

6-(2-methoxy-3-methylphenyl)-2, 4- dimethylnicotinonitrile (2.16) Palladium Charcoal (10%) (6mol%) was added to the well stirred solution of 1-(2-methoxy-3-methylphenyl)but-3-yn-1-ol (50mg, 0.26mmol) in acetonitrile(5ml).After 5min $NaNH_2$ (203mg, 5.2mmol) was added to the solution then the reaction mixture allowed to stirred for 9hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with petroleum ether afforded 6-(2-methoxy-3-methylphenyl)-2, 4-dimethylnicotinonitrile (2.16) as a colourless liquid (33mg, 50 %) R_f = 0.7 in 10 % ethyl acetate in petroleum ether **^{1}H NMR**(400 MHz, $CDCl_3$); 7.71 (s, 1H), 7.57 (dd, *J* = 7.6Hz, 1.6Hz, 1H), 7.29 (d, *J* = 6.4Hz,1H), 7.15 (t, *J* = 7.6Hz, 1H), 3.52 (s, 3H), 2.84 (s, 3H), 2.59 (s, 3H), 2.37 (s, 3H) **^{13}C NMR** (100 MHz,$CDCl_3$) δ =162.8, 159.9, 157.9, 152.5, 134.1, 133.5, 133.3, 130.4, 125.9, 124.1, 118.1, 109.2, 62.3, 25.4, 22.0, 17.5; **IR** (Neat Film, NaCl) 2981, 2230, 1567, 1210, 956 cm^{-1}; **HRMS** (ESI-TOF) m/z: [M + H]+ Calcd for $C_{16}H_{17}N_2O$ 253.1341; Found 253.1337.

6-(3-isobutoxy-4-methoxyphenyl)-2, 4-dimethylnicotinonitrile (2.17) Palladium Charcoal (10%) (6mol%) was added to the well stirred solution of 1-(3-isobutoxy-4-methoxyphenyl)but-3-en-1-ol (80mg,.32mmol) in acetonitrile (8ml).After 5min $NaNH_2$ (250mg, 6.4mmol) was added to the solution then the reaction mixture allowed to stirred for 12hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with petroleum ether afforded 6-(3-isobutoxy-4-methoxyphenyl)-2, 4-dimethylnicotinonitrile

(2.17) as a white solid (46mg, 47 %) R_f = 0.7 in 10 % ethyl acetate in petroleum ether **^{1}H NMR**(400 MHz, $CDCl_3$); 7.65 (d, *J* = 2.4Hz, 1H), 7.57 (dd , *J* = 8.4Hz, 2Hz, 1H), 7.45 (s, 1H), 6.96 (d, *J* = 8.8Hz, 1H), 3.94 (s, 3H), 3.90 (d, *J* = 6.8Hz, 2H), 2.82 (s, 3H), 2.58 (s, 3H), 2.27-2.16 (m, 1H), 1.09 (d, *J* = 6.8Hz, 6H) **^{13}C NMR** (100 MHz,$CDCl_3$) δ = 161.5, 158.5, 151.4, 151.2, 149.0, 143.2, 130.5, 120.2, 117.6, 116.7, 112.1, 111.6, 107.0, 75.5, 56.0, 28.1, 23.9, 20.5, 19.2 ; **IR** (Neat Film, NaCl) 2983, 2220, 1583, 1240, 954 cm^{-1}; **HRMS** (ESI-TOF) m/z: [M + H]+ Calcd $C_{19}H_{23}N_2O_2$ 311.1760 ; Found 311.1752.

6-(4-(benzyloxy)-3-methylphenyl)-2, 4-dimethylnicotinonitrile (2.18) Palladium Charcoal (10%) (6mol%) was added to the well stirred solution of 1-(4-(benzyloxy)-3-methylphenyl)but-3-en-1-ol (70mg, .26mmol) in acetonitrile (7ml). After 5min $NaNH_2$ (203mg, 5.2mmol) was added to the solution then the reaction mixture allowed to stirred for 12hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with petroleum ether afforded 6-(4-(benzyloxy)-3-methylphenyl)-2, 4-dimethylnicotinonitrile (2.18) as a white solid (52mg, 62 %) R_f = 0.5 in 10 % ethyl acetate in petroleum ether **^{1}H NMR**(400 MHz, $CDCl_3$); 7.89-7.83 (m, 2H), 7.48-7.35 (m, 6H), 6.98 (d, *J* = 8.4Hz, 1H), 5.18 (s, 2H), 2.81 (s, 3H), 2.57 (s, 3H), 2.38 (s, 3H) **^{13}C NMR** (100 MHz,$CDCl_3$) δ = 161.5, 158.7, 158.6, 151.2, 136.8, 129.6, 128.4, 127.8, 127.5, 126.9, 126.1, 117.6, 116.8, 111.3, 106.8, 69.7, 23.9, 20.5, 16.4; **IR** (Neat Film, NaCl) 2930, 2226, 1582, 932 cm^{-1} ; **HRMS** (ESI-TOF) m/z: [M + H]+ Calcd for $C_{22}H_{21}N_2O$ 329.1654; Found 329.1648.

6-(2-methoxyphenyl)-2, 4-dimethylnicotinonitrile(2.19) Palladium Charcoal (10%) (6mol%) was added to the well stirred solution of 1-(2-methoxyphenyl)but-3-yn-1-ol (60mg, .34mmol) in acetonitrile (4ml).After 5min $NaNH_2$ (265mg, 6.8mmol) was added to the solution then the reaction mixture allowed to stirred for 12hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with petroleum ether afforded 6-(2-methoxyphenyl)-2, 4-dimethylnicotinonitrile (2.19) as a white solid (49mg, 60 %) R_f = 0.7 in 10 % ethyl acetate in petroleum ether **^{1}H NMR**(400 MHz, $CDCl_3$); 7.81 (dd , *J* = 7.6Hz, 1.6Hz, 1H), 7.66 (s, 1H), 7.44-7.40 (m, 1H), 7.12-7.08 (m, 1H), 7.02 (d, *J* = 8.4Hz, 1H), 3.89 (s, 3H), 2.82 (s, 3H), 2.58 (s, 3H) **^{13}C NMR** (100 MHz,$CDCl_3$) δ = 162.6, 159.3, 158.5, 151.9, 132.7, 132.4, 129.0, 124.7, 122.6, 118.2, 112.8, 108.9, 57.0, 25.4, 22.1 ; **IR** (Neat Film, NaCl) 2950, 2213, 1578, 1230, 950 cm^{-1} ; **HRMS** (ESI-TOF) m/z: [M + H]+ Calcd for $C_{15}H_{15}N_2O$ 239.1184 ; Found 239.1180.

4-ethyl-2-methyl-6-(naphthalen-2-yl)nicotinonitrile(2.20) Palladium Charcoal (10%)(6mol%) was added to the well stirred solution of 1-(naphthalen-2-yl)but-3-yn-1-ol (20mg,.1mmol) in propionitrile (3ml).After 5min $NaNH_2$ (78mg,2mmol) was added to the solution then the reaction mixture allowed to stirred for 12hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with 5% ethyl acetate petroleum ether afforded 4-ethyl-2-methyl-6-(naphthalen-2-yl)nicotinonitrile(2.20) as a yellow liquid (18mg,60 %) R_f = 0.7 in 10 % ethyl acetate in petroleum ether **^{1}H NMR**(400 MHz, $CDCl_3$); 8.62(s, 1H), 8.21(dd, *J* = 8.8Hz, 1.6Hz, 1H), 8.01-7.96(m, 2H), 7.91(t, *J* = 4Hz, 1H), 7.56(t, *J* = 4.8, 3H), 3.07(q, *J* = 7.6Hz, 2H), 2.62(s, 3H), 1.48(t, *J* = 7.6Hz, 3H) **^{13}C NMR** (100 MHz,$CDCl_3$) δ = 172.0, 167.2, 163.6, 134.5, 134.3, 133.2, 130.1, 128.8, 128.5, 127.6, 127.1, 127.0, 126.4, 124.0, 113.6, 32.81, 24.3, 12.9; **IR** (Neat Film, NaCl) 3005, 2218, 1567, 1200, 934 cm^{-1} ; **HRMS** (ESI-TOF) m/z: [M + H]+ Calcd for $C_{19}H_{17}N_2$ 273.1392; Found 273.1381.

6-(4-(allyloxy)-3-methylphenyl)-2-ethyl-4-methylnicotinonitrile (2.21) Palladium Charcoal (10%)(6mol%) was added to the well stirred solution of 1-(4-(allyloxy)-3-methylphenyl)but-3-yn-1ol (90mg, .42mmol) in propionitrile (9ml).After 5min $NaNH_2$ (320mg, 8.2mmol) was added to the solution then the reaction mixture allowed to stirred for 12hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with5% ethyl acetate petroleum ether afforded 6-(4-(allyloxy)-3-methylphenyl)-2-ethyl-4-methylnicotinonitrile (2.21) as a yellow liquid (78mg, 64 %) R_f = 0.7 in 10 % ethyl acetate in petroleum ether **^{1}H NMR**(400 MHz, $CDCl_3$); 7.91 (d, *J* = 8Hz, 2H), 7.32 (s, 1H), 6.91 (d, *J* = 8Hz, 1H), 6.15-6.05 (m, 1H), 5.49-5.30 (m, 2H), 4.64-4.62 (m, 2H), 2.99(q, *J* = 7.9Hz, 2H),2.55 (s, 3H), 2.34 (s, 3H), 1.43 (t, *J* = 7.2Hz, 3H) **^{13}C NMR** (100 MHz,$CDCl_3$) δ =171.7, 166.7, 158.7, 133.0, 129.4, 129.2, 127.2, 125.9, 117.1, 112.5, 111.0, 68.6, 32.7, 24.2, 16.3, 12.9; **IR** (Neat Film, NaCl) 2225, 1612, 1245, 956 cm^{-1} ; **HRMS** (ESI-TOF) m/z: [M + H]+ Calcd for $C_{19}H_{21}N_2O$ 293.1654; Found 293.1652.

6-(2-((4-chlorobenzyl)oxy)-5-methylphenyl)-4-methyl-2-propylnicotinonitrile (2.22) Palladium Charcoal (10%)(6mol%) was added to the well stirred solution of 1-(2-((4-chlorobenzyl)oxy)-5-methylphenyl)but-3-yn-1-ol(69mg,.23mmol) in butonitrile (7ml).After 5min $NaNH_2$ (179.4mg,4.6mmol) was added to the solution then the reaction mixture allowed to stirred for 12hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with 5% ethyl acetate petroleum ether afforded 6-(2-((4-chlorobenzyl)oxy)-5-methylphenyl)-4-methyl-2-propylnicotinonitrile (2.22) as a yellow liquid (55mg, 60%) R_f = 0.7 in 10 % ethyl acetate in petroleum ether**^{1}H NMR** (400 MHz, $CDCl_3$); 7.72 (d, *J* = 2Hz, 1H), 7.55 (s, 1H), 7.37-7.19 (m, 5H), 6.93(d, *J* = 8Hz, 1H),5.09 (s, 2H), 2.98-2.94 (m, 2H), 2.49 (s, 3H), 2.37 (s, 3H), 1.93-1.88 (m, 2H), 1.05 (t, *J* = 7.2Hz, 3H) **^{13}C NMR** (100 MHz,$CDCl_3$) δ = 170.6, 165.9, 162.5, 154.3, 135.2, 133.6, 131.5, 131.4, 131.0, 128.5, 128.3, 127.1, 118.3, 113.2, 70.0, 41.7, 24.1, 22.4, 20.4, 13.9; **IR** (Neat Film, NaCl) 2950, 2218, 1570, 1234, 970 cm^{-1} ; **HRMS** (ESI-TOF) m/z: [M + H]+ Calcd for $C_{24}H_{24}ClN_2O$: 391.1577; Found 391.1571.

2-ethyl-4-methyl-6-(p-tolyl)nicotinonitrile(2.23) Palladium Charcoal (10%)(6mol%) was added to the well stirred solution of 1-(p-tolyl)but-3-yn-1-ol (50mg,.31mmol) in propionitrile (5ml).After 5min $NaNH_2$ (241mg, 6.2mmol) was added to the solution then the reaction mixture allowed to stirred for 9hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with 3% ethyl acetate petroleum ether afforded 2-ethyl-4-methyl-6-(p-tolyl)nicotinonitrile (2.23) as a yellow liquid(40mg,55 %) R_f = 0.7 in 10 % ethyl acetate in petroleum ether **^{1}H NMR**(400 MHz, $CDCl_3$); 7.99 (d, *J* = 8Hz, 2H), 7.36 (s, 1H), 7.30 (d, *J* = 8Hz, 2H), 3.01(q, *J* = 8Hz,2H), 2.56 (s, 3H), 2.43 (s, 3H), 1.43 (t, *J* = 7.6Hz, 3H) **^{13}C NMR** (100 MHz,$CDCl_3$) δ= 171.8, 166.9,

163.6, 140.6, 134.4, 129.4, 126.9, 112.9, 32.7, 24.2, 21.2, 12.8; **IR** (Neat Film, NaCl)2986, 2221, 1617, 1243, 976 cm^{-1} ; **HRMS** (ESI-TOF) m/z: [M + H]+ Calcd for $C_{16}H_{17}N_2$ 237.1392; Found 237.1386.

4-methyl-2-propyl-6-(o-tolyl)nicotinonitrile(2.24) Palladium Charcoal (10%)(6mol%) was added to the well stirred solution of 1-(o-tolyl)but-3-yn-1-ol (70mg, .43mmol) in butonitrile (7ml).After 5min $NaNH_2$ (343.2mg, 8.8mmol) was added to the solution then the reaction mixture allowed to stirred for 7hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with with 5% ethyl acetate petroleum ether petroleum ether afforded 4-methyl-2-propyl-6-(o-tolyl)nicotinonitrile (2.24) as a yellow liquid (65mg, 60 %) R_f = 0.7 in 10 % ethyl acetate in petroleum ether **^{1}H NMR**(400 MHz, $CDCl_3$);7.41-7.29 (m, 4H), 7.10(s, 1H), 2.98-2.94 (m, 2H), 2.57 (s, 3H), 2.41 (s, 3H), 1.95-1.85 (m, 2H), 1.0 3 (t, *J* = 7.6Hz, 3H); **^{13}C NMR** (100 MHz,$CDCl_3$) δ = 170.5, 167.0, 166.6, 138.2, 135.9, 130.9, 129.2, 129.0, 125.9, 117.4, 41.5, 24.2, 27.3, 20.2, 13.9; **IR** (Neat Film, NaCl) 2950, 2216, 1583, 1459, 890 cm^{-1} ; **HRMS** (ESI-TOF) m/z: [M + H]+ Calcd for $C_{17}H_{19}N_2$ 251.1548 ; Found 251.1540.

6-(2-methoxyphenyl)-4-methyl-2-propylnicotinonitrile (2.25) Palladium Charcoal (10%)(6mol%) was added to the well stirred solution of 1-(2-methoxyphenyl)but-3-yn-1-ol (60mg,.34mmol) in butonitrile (4ml).After 5min $NaNH_2$ (266mg,6.8mmol) was added to the solution then the reaction mixture allowed to stirred for 12hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with 5% ethyl acetate petroleum ether petroleum ether afforded 6-(2-methoxyphenyl)-4-methyl-2-propylnicotinonitrile (2.25) as a yellow liquid (50mg, 55 %) R_f = 0.7 in 10 % ethyl acetate in petroleum ether **^{1}H NMR**(400 MHz, $CDCl_3$); 7.93 (dd, *J* = 7.6Hz, 1.6Hz, 1H), 7.57 (s, 1H), 7.45-7.41 (m, 1H), 7.10 (t, *J* = 7.2Hz, 1H), 7.02 (d, *J* = 8Hz, 1H), 3.90 (s, 3H), 2.95 (t, *J* = 7.6Hz, 2H), 2.55 (s, 3H), 1.93-1.88 (m, 2H), 1.04 (t, *J* = 2Hz, 3H) **^{13}C NMR** (100 MHz,$CDCl_3$) δ = 165.9, 162.4, 157.5, 144.2, 139.7, 131.05, 121.0, 118.1, 111.2, 55.4, 41.6, 24.3, 22.3, 13.9 ; **IR** (Neat Film, NaCl) 2912, 2214, 1588, 1234, 946 cm^{-1} ; **HRMS** (ESI-TOF) m/z: [M + H]+ Calcd for $C_{17}H_{19}N_2O$ 267.1497; Found 267.1492.

6-(4-methoxyphenyl)-4-methyl-2-propylnicotinonitrile (2.26) Palladium Charcoal (10%)(6mol%) was added to the well stirred solution of 1-(4-methoxyphenyl)but-3-yn-1-ol (49mg,.28mmol) in butonitrile(4ml).After 5min $NaNH_2$ (219mg, 5.6mmol) was added to the solution then the reaction mixture allowed to stirred for 12hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with 5% ethyl acetate petroleum ether afforded 6-(4-methoxyphenyl)-4-methyl-2-propylnicotinonitrile (2.26) as a yellow liquid (45mg, 60%) R_f = 0.7 in 10 % ethyl acetate in petroleum ether **^{1}H NMR**(400 MHz, $CDCl_3$) 8.06(dd, *J* = 7Hz, 2Hz, 2H), 7.31(s, 2H), 7.00(dd, *J* = 6.8Hz, 2Hz, 2H), 3.87(s, 3H), 2.95-2.91(m, 2H), 2.54(s, 3H), 1.91(q, *J* = 7.6Hz, 2H), 1.04(t, *J* = 7.2Hz, 3H) **^{13}C NMR** (100 MHz,CDCl3) δ = 170.8, 166.7, 163.1, 130.4, 129.6, 128.5, 114.0, 113.5, 112.4, 55.2, 41.5, 24.2, 22.1, 13.9; **IR** (Neat Film, NaCl) 2943, 2214, 1600, 1235, 945 cm^{-1} ; **HRMS** (ESI-TOF) m/z: [M + H]+ Calcd for $C_{17}H_{19}N_2O$ 267.1497; Found 267.1491.

4-methyl-2-propyl-6-(p-tolyl)nicotinonitrile(2.27) Palladium Charcoal (10%) (6mol%) was added to the well stirred solution of 1-(p-tolyl)but-3-yn-1-ol (80mg, .5mmol) in butonitrile(8ml).After 5min $NaNH_2$ (390mg, 10mmol) was added to the solution then the reaction mixture allowed to stirred for 12hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with with 5% ethyl acetate petroleum ether afforded 4-methyl-2-propyl-6-(p-tolyl)nicotinonitrile (2.27) as a yellow liquid (75mg, 60%) R_f = 0.7 in 10 % ethyl acetate in petroleum ether **^{1}H NMR**(400 MHz, $CDCl_3$); 7.99 (d, *J* = 8Hz, 1H), 7.36(s, 1H),7.30 (d, *J* = 8Hz, 1H), 2.97 (m, 1H), 2.55(s, 3H), 2.43(s, 3H),1.95-1.89(m, 2H), 1.04 (t, *J* = 2Hz, 3H) ;) **^{13}C NMR** (100 MHz,$CDCl_3$) δ= 170.9, 166.8, 163.6, 140.6, 134.4, 129.4, 126.9, 113.0, 41.5, 24.2, 22.1, 21.3, 13.9; **IR** (Neat Film, NaCl) 2996, 2210, 1645, 1260, 954 cm^{-1} ; **HRMS** (ESI-TOF) m/z: [M + H]+ Calcd for $C_{17}H_{19}N_2$ 251.1548; Found 251.1542.

6-(4-ethoxy-3,5-dimethylphenyl)-4-methyl-2-propylnicotinonitrile(2.28) Palladium Charcoal (10%) (6mol%) was added to the well stirred solution of 1-(4-ethoxy-3,5-dimethylphenyl)but-3-en-1-ol (30mg,.14mmol) in butonitrile (3ml). After 5min $NaNH_2$ (109mg, 2.8mmol) was added to the solution then the reaction mixture allowed to stirred for 12hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with with 5% ethyl acetate petroleum ether afforded 6-(4-ethoxy-3, 5-dimethylphenyl)-4-methyl-2-propylnicotinonitrile (2.28) as a yellow liquid (28mg, 64%) R_f = 0.7 in 10 % ethyl acetate in petroleum ether **^{1}H NMR**(400 MHz, $CDCl_3$); 7.73 (s, 2H), 7.32 (s, 1H), 3.89 (q, *J* = 6.8Hz, 2H), 2.94 (t, *J* = 7.6Hz, 2H), 2.55 (s, 2H), 2.37 (s, 6H), 1.94-1.87 (m, 2H), 1.45 (t, *J* = 7.2Hz, 3H), 1.04 (t, *J* = 7.2Hz, 3H) **^{13}C NMR** (100 MHz,$CDCl_3$) δ = 170.8, 166.7, 163.6, 158.2, 132.4, 131.4, 131.1, 129.2, 127.6, 113.1, 67.9, 41.6, 24.2, 22.2, 16.4, 15.6, 13.9; **IR** (Neat Film, NaCl) 3010, 2249, 1650, 1256, 939 cm^{-1}; **HRMS** (ESI-TOF) m/z: [M + H]+ Calcd for $C_{20}H_{25}N_2O$ 309.1967; Found 309.1958.

6-(4-(allyloxy)-3-methylphenyl)-4-methyl-2-propylnicotinonitrile (2.29) Palladium Charcoal (10%) (6mol%) was added to the well stirred solution of 1-(4-(allyloxy)-3-methylphenyl)but-3-en-1-ol (79mg, .36mmol) in butonitrile (8ml).After 5min $NaNH_2$ (289mg, 7.2mmol) was added to the solution then the reaction mixture allowed to stirred for 12hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with with 5% ethyl acetate petroleum ether afforded 6-(4-(allyloxy)-3-methylphenyl)-4-methyl-2-propylnicotinonitrile (2.29) as a yellow liquid (68mg, 61%) **^{1}H NMR**(400 MHz, $CDCl_3$); 7.91-7.88 (m, 2H), 7.88 (s, 1H), 6.90 (d, *J* = 9.2Hz, 1H), 6.15-6.05 (m, 1H), 5.49-5.44 (m, 1H), 5.32 (dd, *J* = 10.4Hz, 1.2Hz, 1H), 4.63-4.62 (m, 2H), 2.94 (t, *J* = 7.6Hz, 2H), 2.54 (s, 3H), 2.34 (s, 3H), 1.94-1.89 (m, 2H), 1.04 (t, *J* = 7.6Hz, 3H) **^{13}C NMR** (100 MHz,$CDCl_3$) δ = 170.8, 166.6, 163.4, 158.7, 133.0, 129.4, 129.2, 127.2, 125.9, 117.1, 112.5, 111.0, 68.6, 41.6, 24.2, 22.2, 16.3, 13.9; **IR** (Neat Film, NaCl) 2995, 2232, 1620, 1230, 946 cm^{-1} ;**HRMS** (ESI-TOF) m/z: [M + H]+ for $C_{20}H_{23}N_2O$ 307.1810; Found 307.1803.

2-ethyl-6-(4-methoxyphenyl)-4-methylnicotinonitrile (2.30)

Palladium Charcoal (10%) (6mol%) was added to the well stirred solution of 1-(4-methoxyphenyl)but-3-yn-1-ol (49mg,.28mmol) in propionitrile (5ml).After 5min $NaNH_2$ (219mg, 5.6mmol) was added to the solution then the reaction mixture allowed to stirred for 12hr. The reaction progress was monitored by TLC. Then the mixture was quenched with distilled water and extracted with ethyl acetate (2X3 ml) and dried over sodium sulphate. Solvent was evaporated and the mass was subjected to neutral alumina column, elution with 5% ethyl acetate petroleum ether afforded 2-ethyl-6-(4-methoxyphenyl)-4-methylnicotinonitrile (2.30) as a yellow liquid(38mg, 53 %) R_f = 0.3 in 10 % ethyl acetate in petroleum ether **^{1}H NMR**(400 MHz, $CDCl_3$);8.09 (t, *J* = 6.8Hz, 2H), 7.33 (s, 1H), 7.01 (dd, *J* = 7.2Hz, 1.6Hz, 2H), 3.89 (s, 3H), 2.99(q, *J* = 7.6Hz, 2H), 2.55 (s, 3H), 1.42 (t, *J* = 7.6Hz, 3H) ; **^{13}C NMR** (100 MHz,$CDCl_3$) δ = 171.7, 166.8, 163.2, 161.5, 129.6, 128.5, 114.0, 112.4, 55.2, 32.7, 24.2, 12.8; **IR** (Neat Film, NaCl) 2912, 2244, 1588, 1212, 932 cm^{-1} ; **HRMS** (ESI-TOF) m/z: [M + H]+ for $C_{16}H_{17}N_2O$ 253.1341; Found 253.1337.

ACKNOWLEDGMENT

We sincerely acknowledge Department of Science and Technology (DST), Govt. of India (Grant no. SB/FT/CS-076/2012), Board of Research in Nuclear Sciences (BRNS) (2013/20/37C/2/BRNS/2651) and INSPIRE-DST, Govt. of India (Grant No.04/2013/000751). NR thanks DST for research fellowship .MKG thanks NIT Rourkela for research fellowship. . S.Giri thanks DST-Inspire Award (IFA14-CH-151), Govt. of India for financial support and NIT Rourkela for central computing facilities

ASSOCIATE CONTENT

Supporting information

Copies of ^{1}H and ^{13}C spectra of all new compounds , Computational and Crystal data of new compounds.

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Reference

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28. Crystal handling: mounted on a 50 μm MicroMesh MiTeGen Micromount™ using FROMBLIN Y perfluoropolyether (LVAC 16/6, Aldrich). X-Ray device: Bruker Kappa APEX II CCD-based 4-circle X-ray diffractometer with graphite monochromated Mo K_α radiation (λ = 0.71073 Å) of a fine focus molybdenum-target X-ray tube operating at 50 kV and 30 mA. Crystal data: $C_{18}H_{20}N_2O$, 280.36 g/mol, monoclinic, $P2_1/c$, a = 6.8762(4) Å, b = 14.6452(8) Å, c = 15.4808(9) Å, ß = 101.713(4)°, V = 1526.5(2) $Å^3$, Z = 4, Z' = 1, d_{cal} = 1.220 g/cm^3, T = 100(2) K, μ(Mo K_α) = 0.076 mm^{-1}, F(000) = 600. Data collection: thick, colourless plate of dimension 0.344 x 0.174 x 0.148 mm, $2\Theta_{max}$ = 50°, 39651/2686 reflections collected/unique, completeness to Θ_{max} = 100%, semi-empirical absorption correction from equivalents. Structure refinement: full-matrix least-squares refinement on F^2, 2686 data, 0 restraints, 200 parameters, Goodness-of-fit on F^2 = 1.040, R1 = 0.0502/0.0786, wR2 = 0.1199/0.1361 ($I > 2\sigma(I)$/all data), largest diff. peak and hole = 0.240/-0.180 e/$Å^3$. Programs used: DIAMOND, Brandenburg, K., Crystal Impact GbR, **2006**, Bonn, Germany; SHELXL, Sheldrick, G. M. *Acta Cryst.* **2015**, *C71*, 3–8. CCDC 1544056 contains the supplementary crystallographic data for this paper. The data can be obtained free of

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GRAPHICAL ABSTRACT