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PAPER

A non-metal catalysed oxidation of primary azides to nitriles at ambient temperature†

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A novel non-metal catalyzed oxidation of organic azides to nitriles under solvent-free conditions is presented employing catalytic amounts of KI, and DABCO in aq. TBHP at room temperature. This non-metal catalyzed oxidation of azides provides good selectivity as double and triple bonds were not oxidized under the present reaction conditions.

Introduction

The nitrile functionality has a unique identity in organic synthesis as it can be easily transformed into valuable functional groups such as acids, amines, amides *etc*.[1] Traditionally, aliphatic nitriles are synthesized by employing inorganic cyanides through nucleophilic substitution methods, whereas aromatic nitriles are prepared by Sandmeyer's reaction.[2–5] The search for convenient and useful methods for the synthesis of nitriles has led to novel chemistry as well as newer methods of synthesizing nitriles from a variety of easily available substrates without using inorganic cyanide. Most of the methods that transform alcohols or aldehydes to nitriles use NH_3 as the nitrogen source.[6a,b] Additionally, dehydration of aldoximes or amides to form nitriles is also reported.[6c,d]

Azides are generally considered hazardous. Therefore, the utility of azides, particularly organic azides, has been limited to a greater extent.[7] Generally, azides are used in the Staudinger reaction, Schmidt reaction and Curtius rearrangement.[1f] After the discovery of click chemistry, the utility triazole, which is generated by the reaction of azide and terminal alkynes, as a linker between biomolecules and ligands has led several research groups to re-evaluate the utility of azides in organic synthesis.[8] The contemporary developments, and versatile applications of azides in chemistry, biology, medicine and materials science was reviewed recently by Brase *et al*.[8b]

Efforts in this direction revealed that azides that contain α-hydrogens are useful precursors for the oxidation to the corresponding nitriles. Hence, these strategies turned out to be useful methods to synthesize benzonitriles from the corresponding benzylic azides. Recently, Jiao and co-workers[9] reported copper catalyzed transformation of methylarenes to aryl nitriles and conversion of allylarenes to alkenyl nitriles by employing excess Me_3SiN_3, $FeCl_2$, and DDQ (3 equiv.). These two protocols are specific to methylarenes and allylic systems respectively.[9] Recently, copper catalysed oxidation of aliphatic azides to their corresponding nitriles was reported by our group.[10] Apart from these protocols, ruthenium catalysed aerobic oxidation of aliphatic primary azides to nitriles[11] and BrF_3 promoted transformation of primary azides to the corresponding nitriles[12a] were reported. Interestingly, Pd^0 is known to catalyse decomposition of primary azides to the corresponding nitriles along with amines, and imines as by-products.[12b] Most of these reports utilize either metal catalysts or harsh reaction conditions such as heating the reaction mixture to promote the reaction. Interestingly, iodine compounds[13,14] are used in a variety of oxidative transformations. Hence, there is a surge in the use of iodine and its derivatives as they offer environmentally benign reactions.[14] In this context, we report a selective oxidation of aliphatic primary azides to the corresponding nitriles by employing a catalytic amount of KI using TBHP as the oxidant.

Results and discussion

Initial optimization studies were performed by employing 4-methoxybenzyl azide (**1a**) as the precursor. As seen in Table 1, preliminary investigations were initiated using TBHP as an oxidant. The oxidation of **1a** with a catalytic amount of I_2 and TBHP (3 equiv.) furnished a mixture of corresponding nitrile (**2a**), acid (**3a**) and amide (**4a**) (entry 1, Table 1). To circumvent this problem, further reactions were performed using I_2 and TBHP along with a variety of organic bases. Utility of I_2 either in stoichiometric or catalytic amounts, under solvent-free conditions, furnished a mixture of nitrile (**2a**), acid (**3a**) and amide (**4a**) in the presence of a catalytic amount of pyridine (entries 2 and 3). Further optimization studies with a variety of bases such as triethylamine, DIPEA, DMAP, DABCO resulted in mixture of corresponding nitrile (**2a**), and acid (**3a**) (entries 4–8, Table 1).

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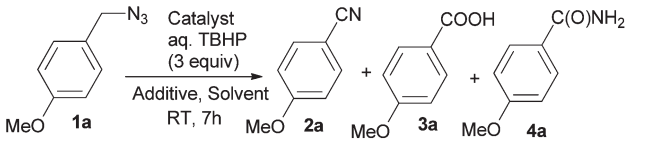
Table 1 Optimization studies



Entry	Catalyst (equiv.)	Additive (equiv.)	Solvent	Yield[a] (%)		
				2a	**3a**[b]	**4a**[b]
1	I_2 (1)	None	Neat	24	64	12
2	I_2 (1)	Pyridine (0.2)	Neat	11	67	18
3	I_2 (0.25)	Pyridine (0.25)	Neat	32	40	28
4	I_2 (0.2)	Et_3N (0.2)	Neat	n.r.		
5	I_2 (0.2)	DIPEA (0.2)	Toluene[c]	20	<5	—
6	I_2 (0.2)	DMAP (0.2)	Toluene[c]	60	<5	—
7	I_2 (0.2)	DABC0 (0.2)	Toluene[c]	64	<5	—
8	I_2 (0.2)	DABCO (1)	Neat	72	<5	—
9	KI (0.25)	None	Neat	70	<5	—
10	KI (0.25)	DABCO (1)	Neat	88	—	—
11	**KI (0.25)**	**DABCO (0.25)**	**Neat**	**88**	—	—
12	KI (0.2)	DABCO (0.25)	Neat	82	—	—
13	KI (0.1)	DABC0 (0.1)	Neat	73	—	—
14	KI (0.1)	DABCO (1)	Neat	72	—	—
15[d]	KI (0.25)	DABCO (0.25)	Neat	66	—	—
16[e]	KI (0.25)	DABCO (0.25)	Neat	60	—	—

[a] Isolated yield. [b] Yield determined by GC. [c] Reaction is carried out at 110 C. [d] Used 2 equiv. of aq. TBHP. [e] Used 1 equiv. of aq. TBHP.

These results suggest that I_2–TBHP system, under the present reaction conditions, is not a suitable combination for the oxidation of azides. As KI is known to react with TBHP to produce I_2, we carried out a few experiments using KI as the iodine source (entries 9–16). As expected, reaction of **1a** with KI (25 mol%) and TBHP (1 equiv.) under solvent-free reaction conditions furnished the corresponding nitrile **2a** in 70% along with trace amount of **3a** (entry 9). Remarkably, the reaction of **1a** with KI (25 mol%), DABCO (1 equiv.) and TBHP (3 equiv.) under solvent-free reaction conditions produced **2a** as the only product (entry 10). Further, experiments using varied amounts of KI, TBHP and DABCO at room temperature (entries 11–16) indicated that the reaction of **1a** with KI (25 mol%), TBHP (3 equiv.) and DABCO (25 mol%) are the most suitable conditions to furnish **2a** in good yield (88%, entry 11).[15] Further, employing a variety of oxidants such as molecular oxygen, H_2O_2, cumene hydroperoxide, oxone, or sodium perborate for the present oxidation did not furnish the nitrile.

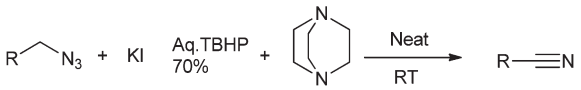
Having established the optimal reaction conditions for the oxidation, we continued our investigation to generalize the results. As can be seen from Table 2, benzyl azide (**1b**) underwent a smooth reaction under the optimized conditions to afford benzonitrile (**2b**) in excellent yield (entry 1, Table 2). The azides bearing methoxy substituents were oxidized to the corresponding nitriles **2c** and **2d** in excellent yields (86% and 89% respectively, entries 2 and 3). Oxidation of 2,4-dichlorobenzyl azide (**1e**) and 4-benzyloxybenzyl azide (**1f**) furnished corresponding nitriles **2e** and **2f** in good yields (81% and 83%, entries 4 and 5). Allyloxy and propargyloxy substituted benzyl azides **1g** and **1h** underwent a facile oxidation to furnish the corresponding nitriles **2g** and **2h** in good yields (entries 6 and 7). Cinnamyl azide **1i** was smoothly transformed to cinnamonitrile **2i** under the standard reaction conditions (85%, entry 8). It is noteworthy that allyl, propargyl, and cinnamyl groups, which are easily amenable for oxidation, are well tolerated under the present reaction conditions. 1-(Azidomethyl)naphthalene **1j** provided the product 1-naphthonitrile **2j** in good yield (entry 9, 79%). Electron withdrawing substituents such as a nitro group at *p*-position of benzyl azide **1k** needed a longer time to produce the corresponding nitrile **2k** in good yield (91%). Similarly, the oxidation of methyl 2-(azidomethyl)benzoate (**1l**) proceeded effectively to furnish the corresponding nitrile **2l** in good yield. The oxidation of heliotropin derived benzyl azide **1m** under standard reaction conditions proceeded efficiently to furnish the corresponding nitrile (**2m**) (85%, entry 12). Despite the fact that 2-(azidomethyl)pyridine needed longer time for the oxidation, the reaction produced good yield of the corresponding nitrile **2n** in 80%, (entry 13). Oxidation of 1-azidoundecane (**1o**) under reflux conditions furnished the corresponding nitrile **2o** in moderate yield. Nevertheless, the sluggish reactivity of aliphatic azide is exploited in demonstrating a chemoselective oxidation of a benzylic azide in the presence of an aliphatic azide. Hence, the oxidation of diazide **1p** under the present reaction conditions resulted in the oxidation of the benzylic azide to nitrile, whereas the aliphatic azido-functionality was inert under the reaction conditions to yield the corresponding ω-azido nitrile **2p** in good yield (77%, entry 15). Similarly, secondary azides under the optimized reaction conditions were unaffected during the reaction.

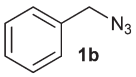
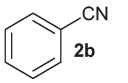
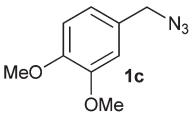
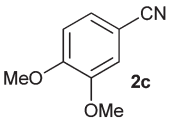
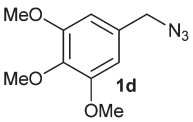
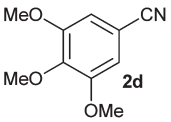
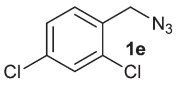
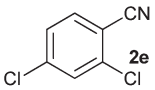
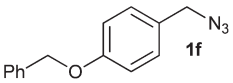
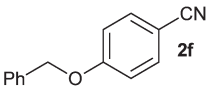
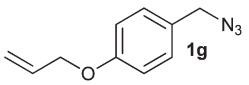
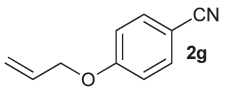
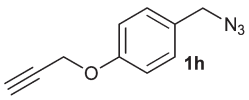
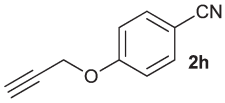
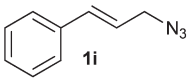
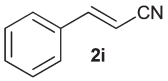
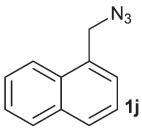
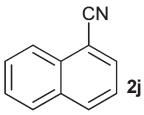
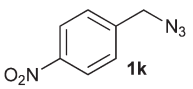
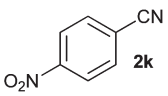
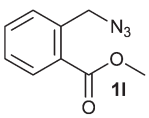
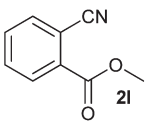
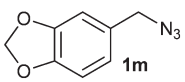
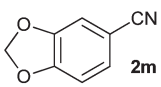
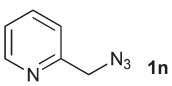
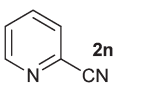
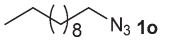
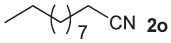
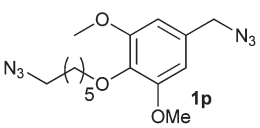
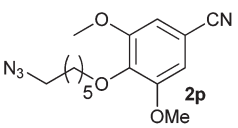
A few experiments were performed to follow the reaction mechanism (Scheme 1). It is well known that the reaction of KI with TBHP produces either hypoiodite[16] or I_2 and KOH.[17] The reaction of I_2 and KOH with *p*-methoxybenzyl azide either at room temperature or at reflux conditions did not furnish the nitrile and the starting material was intact. However, the oxidation of azide **1a** with TBHP and KI under standard reaction conditions in the presence of a radical scavenger BHT (2,6-bis (1,1-dimethylethyl)-4-methylphenol) failed to produce **2a** and the starting material was recovered. This reaction indicates that the reaction is proceeding through a radical intermediate. Based on this preliminary information, we believe that the reaction might go through either *tert*-butoxy radical, or *tert*-butylperoxy radical, which further reacts with azide to form the corresponding nitrile. However, the role of DABCO is not very clear. We believe that DABCO may react with I_2 to generate DABCO salt, which may further react with TBHP to generate *tert*-butoxy radical, or *tert*-butylperoxy radical.[18] This reaction mechanism may be similar to the one that is reported for the oxidation of benzylic amines to the corresponding nitrile.[19] Further work is underway in our laboratory.

Conclusions

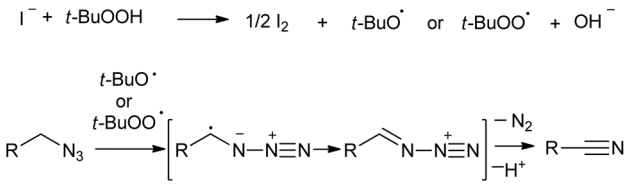
In conclusion we have demonstrated a novel non-metal catalyzed oxidation of organic azides to nitriles under solvent-free conditions. This reaction employs catalytic amounts of KI (25 mol %), DABCO (25 mol%) and aq. TBHP (3 equiv., 70% solution in water) as an oxidant. Besides this, the reaction provide a good selectivity, as double and triple bonds were not oxidized under

Table 2 Oxidation of primary azides to nitriles



Entry	Substrate	Time (h)	Product	Yield (%)[a]
1[b]	 1b	10	 2b	91
2	 1c	7	 2c	86
3	 1d	4	 2d	89
4	 1e	24	 2e	81
5	 1f	18	 2f	83
6	 1g	36	 2g	83
7	 1h	24	 2h	81
8	 1i	8	 2i	85
9	 1j	24	 2j	79
10	 1k	48	 2k	91
11	 1l	48	 2l	83
12	 1m	8	 2m	85
13	 1n	48	 2n	80
14	 1o	24	 2o	51[b]
15	 1p	18	 2p	77

[a] Isolated yield. [b] Yield determined by GC.



Scheme 1 Proposed mechanism for the oxidation of primary azides to nitriles.

the reaction conditions. To the best our knowledge, this is the first report of metal-free oxidation of organic azides to the corresponding nitriles. Additionally, chemoselective oxidation of benzylic azides against aliphatic azides increases the potential application of the present method.

Experimental

Typical experimental procedure for the synthesis of azides[10b]

Benzyl bromide or chloride derivatives (1 mmol) and sodium azide (2 mmol) in acetonitrile (4 mL) were refluxed until completion of the reaction (monitored by TLC). Evaporated the solvent, quenched with water, extracted with Et_2O (3 × 25 mL), combined organic extract was washed with water (3 × 25 mL), dried over Na_2SO_4, concentrated under vacuum. The residue was chromatographed on silica gel with EtOAc : Hexane, 2 : 98 to afford benzyl azide derivatives.

General experimental

NMR spectra were recorded on a JEOL LA-300, BRUKER-AV400 spectrometer in $CDCl_3$, tetramethylsilane (TMS; δ = 0.00 ppm) served as internal standards for ^{1}H NMR. The corresponding residual non-deuterated solvent signal ($CDCl_3$: δ = 77.00 ppm) was used as internal standards for ^{13}C NMR. IR spectra were measured using a JASCO FT/IR-410 spectrometer, and Perkin-Elmer FT/IR Spectrum BX, GX. Mass spectra were measured with Micromass Q-Tof (ESI-HRMS). Column chromatography was conducted on Silica gel 230–400 mesh (Merck) and preparative thin-layer chromatography was carried out using SILICA GEL GF-254.

Typical experimental procedure for the synthesis of nitriles

Typical experimental procedure for 4-methoxybenzonitrile (**2a**): Aqueous TBHP (70% solution in water, 3 mmol) was added dropwise over one minute to a well stirred mixture of 1-(azidomethyl)-4-methoxybenzene (**1a**, 1 mmol), KI (0.25 mmol) and DABCO (0.25 mmol) and stirred at room temperature for 8 h. After completion of the reaction (monitored by TLC), the reaction mixture was quenched with the saturated aq. $Na_2S_2O_3$, and extracted with ethyl acetate (3 × 15 mL). The combined organic layer was washed with dil. HCl (10%, 5 mL), followed by water, dried over anhydrous Na_2SO_4, and the solvent was removed under vacuum to afford the crude product. The crude mixture was purified by column chromatography on silica gel (EtOAc–pet ether 1 : 19 to 1 : 10) to furnish 88% of 4-methoxybenzonitrile (**2a**) as a colorless solid.

Characterization data for azides

1(Azidomethyl)-4-methoxybenzene.[10b] (1a). Colorless liquid; Yield – 90%; R_f (25% EtOAc–hexane) 0.9; IR (Neat, cm^{-1}): 2098; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24 (d, J = 8.28 Hz, 2H), 6.91 (d, J = 8.52 Hz, 2H), 4.26 (s, 2H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.6, 129.7, 127.3, 114.1, 55.2, 54.3, Anal.Calcd for $C_8H_9N_3O$ C, 58.88; H, 5.56; N, 25.75; Found: 58.81; H, 5.82; N, 26.00.

(Azidomethyl)benzene.[10b] (1b). Colorless liquid; Yield – 85%; R_f (25% EtOAc–hexane) 0.9; IR (Neat, cm^{-1}): 2097; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40–7.26 (m, 5H), 4.32 (s, 2H,); ^{13}C NMR (100 MHz, $CDCl_3$): 135.3, 128.8, 128.3, 128.2, 54.8; Anal. Calcd for $C_7H_7N_3$ C, 63.14; H, 5.30; N, 31.56; Found: 62.77; H, 5.36; N, 31.16.

4-(Azidomethyl)-1,2-dimethoxybenzene.[10b] (1c). Pale yellow oil; Yield – 74%; R_f (25% EtOAc–hexane) 0.9; IR (Neat, cm^{-1}): 2096; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.00–6.70 (m, 3H), 4.27 (s, 2H), 3.90 (s, 3H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ:149.1, 149.0, 54.7, 127.7, 120.8, 111.3, 111.00, 55.8, 55.8; GC-MS (m/z): 193 (M^+).

5-(Azidomethyl)-1,2,3-trimethoxybenzene.[20] (1d). Colorless liquid; Yield – 75%; R_f (25% EtOAc–hexane) 0.9; IR (Neat, cm^{-1}): 2101; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.53 (s, 2H), 4.28 (s, 2H), 3.87 (s, 6H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.4, 137.9, 130.9, 105.1, 60.8, 56.1, 55.0; Anal. Calcd for $C_{10}H_{13}O_3N_3$ C, 53.80; H, 5.87; N,18.82; Found: 53.85; H, 6.25; N, 19.17.

1-(Azidomethyl)-2,4-dichlorobenzene (1e).[21] Colorless liquid; Yield – 90%; R_f (25% EtOAc–hexane) 0.9; IR (Neat, cm^{-1}): 2105; ^{1}H NMR (400 MHz, $CDCl_3$): 7.42 (d, J = 2 Hz, 1H), 7.34–7.32 (m, 1H), 7.29–7.26 (m, 1H), 4.46 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 134.8, 134.4, 131.9, 130.7, 129.6, 127.4, 51.7; Anal. Calcd for $C_7H_5Cl_2N_3$ C, 41.61; H, 2.49; N, 20.80; Found: C, 41.26; H, 2.83; N, 20.98.

1-(Azidomethyl)-4-(benzyloxy)benzene.[22] (1f). White Solid; Yield – 75%; *mp*: 35–37 °C (lit.[21] 35 °C); R_f (25% EtOAc–hexane) 0.9; IR (Neat, cm^{-1}): 2097; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43–7.30 (m, 5H), 7.23 (d, J = 8.56 Hz, 2H), 6.97 (d, J = 8.60 Hz, 2H), 5.06 (s, 2H), 4.25 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.8, 136.8, 129.7, 128.6, 127.9, 127.7, 127.4, 115.1, 70.0, 54.3; Anal. Calcd for $C_{14}H_{13}ON_3$ C, 70.28; H, 5.48; N, 17.56; Found: C, 70.47; H, 5.68; N, 17.93.

1-(Allyloxy)-4-(azidomethyl)benzene (1g). Colorless liquid; Yield – 85%; R_f (25% EtOAc–hexane) 0.9; IR (Neat, cm^{-1}): 2098; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23 (d, J = 8.60 Hz, 2H), 6.92 (d, J = 8.68 Hz, 2H), 6.10–6.00 (m, 1H), 5.41 (dd, J_1 = 1.6 Hz, J_2 = 17.28 Hz, 1H), 5.29 (dd, J_1 = 1.4 Hz, J_2 = 10.48 Hz, 1H), 4.54 (dt, J_1 = 1.52 Hz, J_2 = 5.28 Hz, 2H) 4.26 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.6, 133.0, 129.7, 127.5, 117.7, 114.9, 114.8, 68.8, 54.4; Anal. Calcd for $C_{10}H_{11}N_3O$ C, 63.48; H, 5.86; N, 22.21; Found: C, 63.48; H, 5.90; N, 22.14.

1-(Azidomethyl)-4-(prop-2-yn-1-yloxy)benzene.[23] (1h). Pale yellow liquid; Yield – 81%; R_f (25% EtOAc–hexane) 0.8; IR (Neat, cm^{-1}) 2098 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.25 (d, J = 8.6 Hz, 2H), 6.98 (d, J = 8.6 Hz, 2H), 4.69 (d, J = 2.28 Hz, 2H), 4.27 (s, 2H), 2.53 (t, J = 2.36 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.5, 129.6, 128.3, 115.1, 78.3, 77.3, 76.9, 76.7, 75.7, 55.7, 54.2; Anal. Calcd for $C_{10}H_9N_3O$ C, 64.16; H, 4.85; N, 22.45; Found: 63.80; H, 5.12; N, 22.21.

(3-Azidoprop-1-en-1-yl) benzene.[10b] (1i). Pale yellow liquid; Yield – 75%; R_f (25% EtOAc–hexane) 0.9; IR (Neat, cm^{-1}) 2098; ^1H NMR (400 MHz, $CDCl_3$): δ 7.40–7.23 (m, 5H), 6.64 (d, J = 15.8 Hz, 1H), 6.23 (dt, J_1 = 6.6 Hz, J_2 = 15.72 Hz, 1H), 3.93 (d, J = 6.56 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.9, 134.5, 128.6, 128.1, 126.6, 122.3, 52.9; Anal. Calcd for $C_9H_9N_3$ C, 67.90; H, 5.70; N, 26.40; Found: 67.73; H, 5.81; N, 26.04.

1-(Azidomethyl)naphthalene.[10a] (1j). Colorless liquid Yield – 80%; R_f (25% EtOAc–hexane) 0.8; IR (Neat, cm^{-1}): 2099; ^1H NMR (400 MHz, $CDCl_3$): δ 8.0 (d, J = 8 Hz, 1H), 7.87–7.81 (m, 2H), 7.57–7.48 (m, 2H), 7.44–7.41 (m, 2H), 4.71 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 133.8, 131.3, 130.9, 129.3, 128.7, 127.2, 126.6, 126.1, 125.1, 123.4, 52.9; Anal. Calcd for $C_{11}H_9N_3$ C, 72.11; H, 4.95; N,22.94; Found: C, 72.08; H, 4.99; N, 22.66.

1-(Azidomethyl)-4-nitrobenzene.[24] (1k). Pale yellow liquid; Yield – 92%; R_f (25% EtOAc–hexane) 0.8; IR (Neat, cm^{-1}): 2099; ^1H NMR (400 MHz, $CDCl_3$): 8.24 (d, J = 8.52 Hz, 2H), 7.50 (d, J = 8.48 Hz, 2H), 4.51 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.7, 142.7, 128.5, 123.9, 53.7; Anal. Calcd for $C_7H_6N_4O_2$, C, 47.19; H, 3.39; N, 31.45; Found: C, 47.35; H, 3.72; N, 30.86.

Methyl 2-(azidomethyl)benzoate.[10b] (1l). Pale yellow liquid; Yield – 76%; R_f (25% EtOAc–hexane) 0.8; IR (Neat, cm^{-1}): 2103, 1719; ^1H NMR (400 MHz, $CDCl_3$): δ 8.02 (dd, J_1 = 1.24 Hz, J_2 = 7.84 Hz, 1H), 7.55 (dt, J_1 = 1.44 Hz, J_2 = 7.64 Hz, 1H), 7.49–7.47 (m, 1H), 7.40 (dt, J_1 = 1.44 Hz, J_2 = 7.68 Hz, 1H), 4.81 (s, 2H), 3.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.0, 137.3, 132.6, 131.1, 129.7, 128.7, 128.0, 53.1, 52.3; HRESI-MS (*m/z*): Calculated for $C_9H_9N_3O_2$ (M + Na): 214.0592, found (M + Na): 214.0554.

5-(Azidomethyl)benzo[*d*][1,3]dioxole.[20] (1m). Colorless liquid; Yield – 83%; R_f (25% EtOAc–hexane) 0.8; IR (Neat, cm^{-1}): 2097; ^1H NMR (400 MHz, $CDCl_3$): δ 6.80 – 6.76 (m, 3H), 5.97 (s, 2H), 4.22 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.0, 147.6, 129.0, 121.9, 108.7, 108.3, 101.2, 54.7; Anal. Calcd for $C_8H_7O_2N_3$ C, 54.24; H, 3.98; N, 23.72; Found: C, 54.79; H, 4.37; N, 23.83.

2-(Azidomethyl)pyridine.[25] (1n). Colorless oil; Yield – 85%; R_f (25% EtOAc–hexane) 0.5; IR (Neat, cm^{-1}): 2103; ^1H NMR (400 MHz, $CDCl_3$): δ 8.60–8.59 (m, 1H), 7.71 (td, J_1 = 1.8 Hz, J_2 = 7.68 Hz, 1H), 7.34 (d, J = 7.76 Hz, 1H,), 7.25–7.22 (m, 1H), 4.49 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.6, 149.6, 136.9, 122.8, 121.9, 55.6; Anal. Calcd for $C_6H_6N_4$ C, 53.72; H, 4.51; N, 41.77; Found: C, 53.75; H, 4.95; N, 41.59.

2-(6-Azidomethyl)oxy-5-(azidomethyl)-1,3-dimethoxybenzene (1o)

Colorless liquid; Yield – 75%; R_f (25% EtOAc–hexane) 0.7; Prepared as shown in general Scheme 1. IR (Neat, cm^{-1}): 2097; ^1H NMR (400 MHz, $CDCl_3$): δ 6.52 (s, 2H), 4.28 (s, 2H), 3.96 (t, J = 6.6 Hz, 2H), 3.85 (s, 6H), 3.28 (t, J = 6.92 Hz, 2H), 1.79–1.72 (m, 2H), 1.65–1.60 (m, 2H), 1.53–1.43 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.4, 137.1, 130.7, 105.2, 73.1, 56.1, 55.1, 51.4, 29.9, 28.8, 26.5, 25.4; HRESI-MS (*m/z*): Calculated for $C_{15}H_{22}N_6O_3$ (M + Na): 357.1651, found (M + Na): 357.1653.

Characterisation data for nitriles

4-Methoxybenzonitrile.[9a] (2a). Colorless solid; Yield – 88%; *mp*: 55–57 °C (lit.[3] 56–57 °C); R_f (25% EtOAc–hexane) 0.50; Prepared as given in general experimental procedure. IR (Neat, cm^{-1}): 2219; ^1H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, J = 8.9 Hz, 2H), 6.95 (d, J = 8.9 Hz, 2H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.8, 133.9, 119.2, 114.7, 103.9, 55.5; HRESI-MS (*m/z*): Calculated for C_8H_7NO (M + Na): 156.0425, found (M + Na): 156.0427.

3,4-Dimethoxybenzonitrile.[9a] (2c). Colorless solid; Yield – 86%; *mp*: 63–65 °C (lit.[3] 65–66 °C); R_f (25% EtOAc–hexane) 0.50; Prepared as given in the general experimental procedure. IR (Neat, cm^{-1}) 2224.0; ^1H NMR (400 MHz, $CDCl_3$): δ 7.29 (d, J = 8.12 Hz, 1H), 7.08 (s, 1H), 6.91 (d, J = 8.32 Hz, 1H), 3.94 (s, 3H), 3.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.8, 149.1, 126.4, 119.2, 113.8, 111.1, 103.8, 56.1, 56.0; HRESI-MS (*m/z*): Calculated for $C_9H_9NO_2$ (M + Na): 186.0531, found (M + Na): 186.0532.

3,4,5-Trimethoxybenzonitrile.[6a] (2d). Colorless solid; Yield – 89%; *mp*: 93–95 °C (lit.[3] 92–94 °C); R_f (25% EtOAc–hexane) 0.50; Prepared as given in the general experimental procedure. IR (Neat, cm^{-1}) 2224.0; ^1H NMR (400 MHz, $CDCl_3$): δ 6.86 (s, 2H), 3.90 (s, 3H), 3.88 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.5, 142.3, 118.9, 109.4, 106.7, 61.0, 56.3; HRESI-MS (*m/z*): Calculated for $C_{10}H_{11}NO_3$ (M + Na): 216.0637, found (M + Na): 216.0644.

2,4-Dichlorobenzonirtile.[26] (2e). Colorless solid; Yield – 81%; *mp*: 56–59 °C (lit.[3] 58–61 °C); R_f (25% EtOAc–hexane) 0.50; Prepared as given in the general experimental procedure. IR (Neat, cm^{-1}) 2224.0; ^1H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, J = 8.32 Hz, 1H), 7.55 (d, J = 1.56 Hz, 1H), 7.38 (dd, J_1 = 1.6 Hz, J_2 = 8.36 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.1, 137.8, 134.6, 130.2, 127.8, 115.2, 111.8; HRESI-MS (*m/z*): Calculated for $C_7H_3Cl_2N$ (M + H): 171.9721, found (M + H): 171.9730.

4-(Benzyloxy)benzonitrile.[27] (2f). Colorless solid; Yield – 83%; *mp*: 93–95 °C; R_f (25% EtOAc–hexane) 0.5; Prepared as given in the general experimental procedure. IR (Neat, cm^{-1}): 2217; ^1H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, J = 8.80 Hz, 2H), 7.41–7.35 (m, 5H), 7.02 (d, J = 8.76 Hz, 2H), 5.11 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.9, 135.6, 134.0, 128.7, 128.4, 127.4, 119.1, 115.5, 104.1, 70.2; HRESI-MS (*m/z*): Calculated for $C_{14}H_{11}NO$ (M + Na): 232.0738, found (M + Na): 232.0757.

4-(Allyloxy)benzonitrile.[28] (2g). Colorless solid; Yield – 83%; *mp*: 43–46 °C (lit.[3] 43–44 °C); R_f (25% EtOAc–hexane) 0.5; Prepared as given in the general experimental procedure. IR (Neat, cm^{-1}): 2223.73; ^1H NMR (400 MHz, $CDCl_3$): δ 7.57 (d, J = 8.76 Hz, 2H), 6.96 (d, J = 8.72 Hz, 2H), 6.08–5.98 (m, 1H), 5.42 (d, J = 17.24 Hz, 1H), 5.33 (d, J = 10.52 Hz, 1H), 4.59 (dd, J_1 = 0.92 Hz, J_2 = 5.36 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.8, 133.9, 132.0, 119.1, 118.4, 115.3, 104.0, 69.0; HRESI-MS (*m/z*): Calculated for $C_{10}H_9NO$ (M + Na): 182.0582, found (M + Na): 182.0597.

Cinnamonitrile.[6a] (2h). Colorless liquid; Yield – 85%; R_f (25% EtOAc–hexane) 0.50; Prepared as shown in general experimental procedure. IR (Neat): 2218 cm^{-1}, ^1H NMR (400 MHz, $CDCl_3$): δ 7.46–7.37 (m, 6H), 5.87 (d, J = 16.68 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.5, 133.5, 131.2, 129.1, 127.3, 118.1, 96.3; HRESI-MS (*m/z*): Calculated for C_9H_7N (M + H): 130.0657, found (M + H): 130.0644.

4-(Prop-2-yn-1-yloxy)benzonitrile (2i). Colorless solid; Yield – 81%; *mp*: 111–113 °C; R_f (25% EtOAc–hexane) 0.5; Prepared as shown in general experimental procedure. IR (Neat, cm^{-1}): 2223; ^1H NMR (400 MHz, $CDCl_3$): δ 7.61 (d, J = 8.8 Hz, 2H), 7.04 (d, J = 8.76 Hz, 2H), 4.76 (d, J = 2.12 Hz, 2H), 2.57 (t, J = 2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.6, 133.9, 118.9, 115.6, 104.9, 76.7, 76.5, 55.9; HRESI-MS (*m/z*): Calculated for $C_{10}H_7NO$ (M + H): 158.0606, found (M + H): 158.0602.

1-Naphthonitrile.[6a] (2j). Colorless solid; Yield – 79%; *mp*: 55–57 °C (lit.[3] 56–58 °C); R_f (25% EtOAc–hexane) 0.5; Prepared as given in the general experimental procedure. IR (Neat, cm^{-1}); 2222; ^1H NMR (400 MHz, $CDCl_3$): δ 8.24 (d, J = 8.28 Hz, 1H), 8.08 (d, J = 8.28 Hz, 1H), 7.93–7.90 (m, 2H), 7.70 (t, J = 7.68 Hz, 1H), 7.62 (t, J = 7.28 Hz, 1H), 7.53 (t, J = 7.72 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 133.3, 132.9, 132.6, 132.3, 128.6, 128.5, 127.5, 125.1, 124.9, 117.8, 110.1; HRESI-MS (*m/z*): Calculated for $C_{11}H_7N$ (M + H): 154.0657, found (M^+): 154.0648.

4-Nitrobenzonitrile.[6a] (2k). Colorless solid; Yield – 91%; *mp*: 147–149 °C (lit.[3] 148–149 °C); R_f (25% EtOAc–hexane) 0.5; Prepared as given in the general experimental procedure. IR (Neat, cm^{-1}); 2222; ^1H NMR (400 MHz, $CDCl_3$): δ 8.37 (d, J = 8.96 Hz, 2H), 7.90 (d, J = 8.92 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.0, 133.4, 124.2, 118.3, 116.8; Anal. Calcd for $C_7H_4N_2O_2$ C, 56.76; H, 2.72; N, 18.91; Found: C, 56.67; H, 3.26; N, 19.14.

Methyl 2-cyanobenzoate.[29] (2l). Colorless solid; Yield – 83%; *mp*: 50–53 °C (lit.[3] 50–52 °C); R_f (25% EtOAc–hexane) 0.4; Prepared as given in the general experimental procedure. IR (Neat, cm^{-1}); 2229; ^1H NMR (400 MHz, $CDCl_3$): δ 8.16–8.14 (m, 1H), 7.83–7.81 (m, 1H), 7.71–7.65 (m, 2H), 4.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.5, 134.8, 132.7, 132.5, 132.4, 131.2, 117.5, 112.9, 52.8; HRESI-MS (*m/z*): Calculated for $C_9H_7NO_2$ (M + Na): 184.0374, found (M + Na): 184.0382.

Benzo[*d*][1,3]dioxole-5-carbonitrile.[30] (2m). Colorless solid; Yield – 82%; *mp*: 89–92 °C (lit.[3] 90–93 °C); R_f (25% EtOAc–hexane) 0.5; Prepared as given in the general experimental procedure. IR (Neat, cm^{-1}); 2226; ^1H NMR (400 MHz, $CDCl_3$): δ 7.21 (d, J = 8.04 Hz, 1H), 7.03 (s, 1H), 6.86 (d, J = 8.08 Hz, 1H), 6.07 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.5, 147.9, 128.2, 118.9, 111.3, 109.1, 104.9, 102.2; HRESI-MS (*m/z*): Calculated for $C_8H_5NO_2$ (M + H): 148.0399, found (M + H): 148.0394.

Pyridine-2-carbonitrile.[31] (2n). Colorless solid; Yield – 80%; *mp*: 46–49 °C (lit.[3] 45–48 °C); R_f (25% EtOAc–hexane) 0.4; Prepared as given in the general experimental procedure. IR (Neat, cm^{-1}); 2221.5; ^1H NMR (400 MHz, $CDCl_3$): δ 8.74 (d, J = 4.48 Hz, 1H), 7.87 (t, J = 7.76 Hz, 1H), 7.72 (d, J = 7.72 Hz, 1H), 7.55 (t, J = 5.48 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.1, 137.0, 134.0, 128.5, 126.9, 117.1069; HRESI-MS (*m/z*): Calculated for $C_6H_4N_2$ (M + H): 105.0453, found (M + H): 105.0461.

4-((6-Azidohexyl)oxy)-3,5-dimethoxybenzonitrile (2p). Colorless Liquid; Yield – 77%; R_f (25% EtOAc–hexane) 0.6; Prepared as given in the general experimental procedure. IR (Neat, cm^{-1}); 2226.9, 2094.4; ^1H NMR (400 MHz, $CDCl_3$): δ 6.85 (s, 2H), 4.02 (t, J = 6.56 Hz, 2H), 3.86 (s, 6H), 3.28 (t, J = 6.88 Hz, 2H), 1.79–1.72 (m, 2H), 1.67–1.60 (m, 2H), 1.53–1.41 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.8, 141.7, 119.0, 109.5, 106.5, 73.4, 56.3, 51.4, 29.9, 28.8, 26.4, 25.3; HRESI-MS (*m/z*): Calculated for $C_{15}H_{20}N_4O_3$ (M + Na): 327.1433, found (M + H): 327.1432.

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