A highly efficient heterogeneous ruthenium-catalysed oxidative α-cyanation of tertiary amines leading to α-aminonitriles

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Oxidative α-cyanation of tertiary amines was achieved by using an MCM-41-immobilised *N*-alkylethylenediamine ruthenium(III) complex (MCM-41-2N-$RuCl_3$) as catalyst in MeOH at 60 ºC in the presence of H_2O_2 as oxidant and NaCN in acetic acid as a cyanide source to afford the corresponding α-aminonitriles in good yields. The new heterogeneous ruthenium catalyst can easily be prepared by a simple two-step procedure from commercially readily available and inexpensive reagents. It can be recovered by filtration of the reaction solution and reused at least 7 times without significant loss of activity.

Keywords: supported ruthenium catalyst, oxidative α-cyanation, α-aminonitrile, MCM-41, heterogeneous catalysis

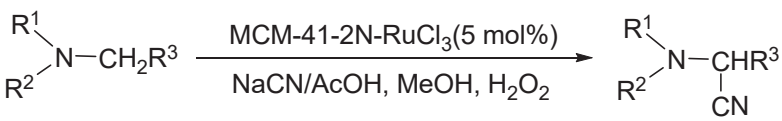
α-Aminonitriles are highly useful and versatile synthetic intermediates and have been widely utilised in the construction of biologically active nitrogen compounds such as alkaloids.[1,2] The traditional methods for the synthesis of α-aminonitriles include the Strecker reaction,[3,4] the oxidative cyanation of secondary[5] or tertiary[6,7] amines and anodic oxidative cyanation of tertiary amines.[8] However, most of these methods suffer from one or more limitations, such as poor selectivity, multistep synthesis, limited substrate scope, heavy metal oxidants and generation of huge amount of wastes, which limit their application. Recently, transition metal-catalysed direct oxidative cyanation of C–H bonds in tertiary amines has provided a simple and straightforward approach for the preparation of these compounds. So far, a number of metal catalysts including Ru,[9–14] Fe,[15–18] V,[19] Mo,[20] Au[21,22] and Re[23] in the presence of oxidants such as H_2O_2, *tert*-butyl hydroperoxide (TBHP) and O_2 have been reported for the direct oxidative α-cyanation of tertiary amines. However, in most cases, homogeneous metal catalysts were used and the use of expensive metals such as ruthenium, rhenium and gold as well as difficult recovery and non-recyclability of the metal catalysts make these methods of limited synthetic utility from environmental and economic points of view. Therefore, development of an efficient, economic and practical method for the direct synthesis of α-aminonitriles through the oxidative α-cyanation of tertiary amines is highly desirable.

Separation and recycling of homogeneous catalysts are tasks of great economic and environmental importance in the chemical and pharmaceutical industries, especially when expensive and/or toxic heavy metal complexes are utilised.[24] Immobilisation of homogeneous catalysts on various solid supports, especially porous materials with high surface areas, is usually the method of choice because the supported catalysts can easily be recovered by a simple filtration of the reaction solution. The discovery of mesoporous material MCM-41 has provided a new possible candidate for an ideal heterogeneous support for immobilising homogeneous catalysts.[25,26] To date, some functionalised MCM-41-immobilised palladium,[27–29] rhodium,[30] molybdenum,[31] gold[32] and copper[33–35] complexes have been successfully utilised as potentially green and sustainable catalysts in organic reactions. In continuation of our efforts to develop efficient, cost-effective and environmentally friendly synthetic pathways for organic transformations,[29,33–35] we wish to report here the first synthesis of an MCM-41-immobilised *N*-alkylethylenediamine Ru(III) complex (MCM-41-2N-$RuCl_3$) and its successful application to oxidative α-cyanation of tertiary amines in the presence of H_2O_2 as oxidant and NaCN in acetic acid as a cyanide source (Scheme 1). To the best of our knowledge, this is the first example of using a heterogeneous ruthenium complex for the oxidative α-cyanation of tertiary amines with high efficiency. The new catalyst could be easily recovered from the reaction mixture by a simple filtration of the reaction solution and its catalytic efficiency remained unaltered even after recycling seven times.

Results and discussion

The new MCM-41-supported *N*-alkylethylenediamine ruthenium(III) complex (MCM-41-2N-$RuCl_3$) was prepared from commercially readily available reagents according to the procedure summarised in Scheme 2. Firstly, the mesoporous material MCM-41 was treated with 3-(2-aminoethylamino)-propyltrimethoxysilane in toluene at 100 °C for 24 h, followed by silylation with Me_3SiCl in toluene at room temperature for 24 h to afford 3-(2-aminoethylamino)propyl-functionalised MCM-41 (MCM-41-2N). The latter was subsequently reacted with $RuCl_3$ in acetone under reflux for 72 h to give the MCM-41-supported *N*-alkylethylenediamine ruthenium(III) complex (MCM-41-2N-$RuCl_3$) as a grey powder. The ruthenium content of the complex was found to be 0.47 mmol g^{-1} according to inductively coupled plasma atom emission spectrometry (ICP-AES) measurements and details of XRD, EDS and XPS studies are given in the Electronic Supplementary Information. Scheme 2 shows a reasonable proposal for the structure of the complex.

The MCM-41-immobilised *N*-alkylethylenediamine ruthenium(III) complex (MCM-41-2N-$RuCl_3$) was then used as catalyst for the oxidative α-cyanation reaction of tertiary



Scheme 1

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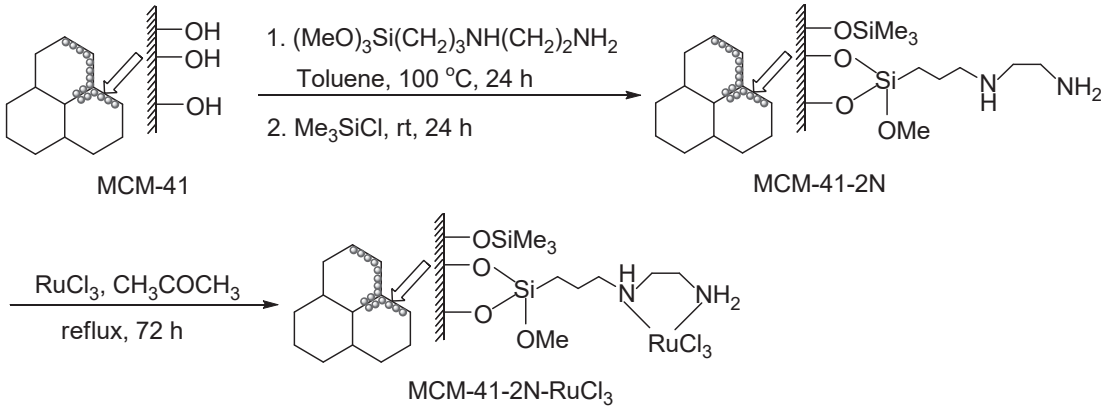
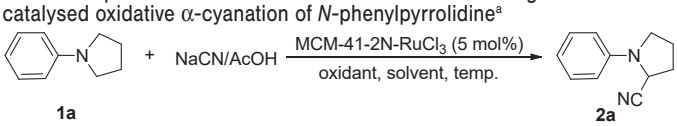


Scheme 2

Table 1 Optimisation of reaction conditions for heterogeneous Ru-catalysed oxidative α-cyanation of *N*-phenylpyrrolidine[a]



1a 2a

Entry	Oxidant	Solvent	Temp. (°C)	Time (h)	Yield (%)[b]
1	H_2O_2[c]	MeOH	25	24	0
2	H_2O_2	MeOH	40	24	48
3	H_2O_2	MeOH	60	4	85
4	H_2O_2	MeOH	70	3	81
5	TBHP	MeOH	60	24	46
6	O_2 (1 atm)	MeOH	60	24	24
7	–	MeOH	60	24	0
8	H_2O_2	EtOH	60	6	79
9	H_2O_2	*i*-PrOH	60	24	37
10	H_2O_2	EtOAc	60	24	35
11	H_2O_2	MeCN	60	24	18
12[d]	H_2O_2	MeOH	60	2	84
13[e]	H_2O_2	MeOH	60	10	64

[a]Reaction conditions: *N*-phenylpyrrolidine (1.0 mmol), NaCN (1.2 mmol), AcOH (6.0 mmol), oxidant (2.5 mmol), MCM-41-2N-$RuCl_3$ (5 mol%), solvent (2 mL) under Ar.

[b]Isolated yield.

[c]30% H_2O_2 aqueous solution.

[d]10 mol% Ru catalyst was used.

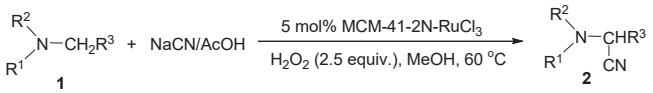
[e]2 mol% Ru catalyst was used.

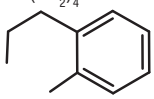
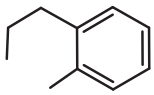
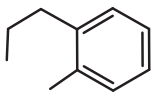
amines with NaCN in acetic acid as a cyanide source. In our initial screening experiments, the oxidative α-cyanation of *N*-phenylpyrrolidine (**1a**) catalysed by MCM-41-2N-$RuCl_3$ was selected as the model reaction to optimise the reaction conditions and the results are summarised in Table 1 (see CAUTION in the Experimental section). At first, the temperature effect was examined in MeOH with hydrogen peroxide as oxidant and a significant temperature effect was observed (Table 1, entries 1–4). It is evident that the reaction did not occur at room temperature and the reaction run at 40 ºC gave a low yield. When the temperature was raised to 60 ºC, the desired product **2a** was isolated in 85% yield. Our next studies focused on the effect of various oxidants on the model reaction. When other oxidants such as TBHP or molecular oxygen were used, the reaction proceeded slowly and only low yields were obtained (Table 1, entries 5 and 6). So hydrogen peroxide, which satisfies environmental and sustainability demands, was found to be the best oxidant for this transformation (Table 1, entry 3). However, no reaction occurred in the absence of an oxidant (Table 1, entry 7). Among the various solvents such as EtOH, MeOH, *i*-PrOH, EtOAc and MeCN tested (Table 1, entries 3 and 8–11), MeOH gave the best result. Finally, the catalyst amount was also screened and the use of 5 mol% catalyst was found to be optimal. A lower yield was observed when the catalyst amount was reduced to 2 mol% (Table 1, entry 13). Therefore, the optimal catalytic system involved the use of MCM-41-2N-$RuCl_3$ (5 mol%) in MeOH with H_2O_2 as oxidant at 60 °C under Ar for 4 h (Table 1, entry 3). The reaction also worked well under N_2 but a decreased yield was observed in air.

With the optimal conditions for the highly efficient and selective oxidative cyanation of tertiary amines in hand, we started to investigate the scope of this heterogeneous ruthenium-catalysed reaction by using different tertiary amines as substrates and the results are summarised in Table 2. To our delight, all the substrates were selectively and effectively converted into the corresponding α-aminonitriles in good yields. Substituted *N*-phenylpyrrolidines **1b** and **1c** afforded the desired products **2b** and **2c** in 81 and 78% yields respectively (Table 2, entries 2 and 3). Other cyclic tertiary amines such as *N*-arylpiperidines **1d–f** and *N*-aryltetrahydroisoquinolines **1g–i** were also suitable substrates and could undergo the cyanation reaction effectively to give the corresponding cyanated products **2d–i** in 68–82% yields (Table 2, entries 4–9). Furthermore, the reaction can also be applied to many acyclic tertiary amines. As shown in Table 2, the reactions of *N,N*-dimethylaniline (**1j**) and substituted *N,N*-dimethylanilines **1k–t** bearing either electron-donating or electron-withdrawing substituents proceeded smoothly to give the corresponding cyanated products **2j–t** in 64–86% yields (Table 2, entries 10–20). A variety of functional groups such as methyl, methoxy, fluoro, chloro, bromo, cyano, nitro, ester, alkynyl and ketone were tolerated well. The results indicated that the electronic nature of the substituent on the benzene ring has limited influence on this heterogeneous ruthenium-catalysed oxidative α-cyanation reaction. It is noteworthy that bulky *N,N*-dimethyl-1-naphthylamine (**1u**) also afforded the expected product **2u** in 76% yield (Table 2, entry 21) and *N*-ethyl-*N*-methylaniline (**1v**), an unsymmetrical aniline, underwent a regioselective oxidative cyanation at the methyl group rather than at the methylene carbon of the ethyl group to furnish the desired product **2v** in 65% yield (Table 2, entry 22).

To verify whether the observed catalysis was due to the heterogeneous ruthenium catalyst or to a leached ruthenium species in solution, we performed the hot filtration test.[36] We focused on the oxidative α-cyanation of *N*-phenylpyrrolidine (**1a**). We filtered off the MCM-41-2N-$RuCl_3$ complex after 2 h of reaction time and allowed the filtrate to react further at 60 °C. The catalyst filtration was performed at the reaction temperature (60 °C) to avoid possible re-coordination or precipitation of soluble ruthenium upon cooling. We found that, after this hot filtration, no significant increase in conversion was

Table 2 Heterogeneous Ru-catalysed oxidative α-cyanation of tertiary anilines[a]



Entry	R^1–	R^2–	R^3–	Product	Yield (%)[b]
1	Ph–	–$(CH_2)_3$–		**2a**	85
2	*o*-MeC_6H_4–	–$(CH_2)_3$–		**2b**	81
3	*p*-$MeOC_6H_4$–	–$(CH_2)_3$–		**2c**	78
4	Ph–	–$(CH_2)_4$–		**2d**	73
5	*p*-$MeOC_6H_4$–	–$(CH_2)_4$–		**2e**	75
6	*o*-$NO_2C_6H_4$–	–$(CH_2)_4$–		**2f**	68
7	Ph–			**2g**	82
8	*m*-MeC_6H_4–			**2h**	77
9	*p*-BrC_6H_4–			**2i**	75
10	Ph–	Me–	H–	**2j**	86
11	*p*-MeC_6H_4–	Me–	H–	**2k**	82
12	*m*-MeC_6H_4–	Me–	H–	**2l**	80
13	*p*-BrC_6H_4–	Me–	H–	**2m**	75
14	*m*-ClC_6H_4–	Me–	H–	**2n**	71
15	*p*-CNC_6H_4–	Me–	H–	**2o**	67
16	*p*-PhC_6H_4–	Me–	H–	**2p**	78
17	*p*-(4-FC_6H_4)C_6H_4–	Me–	H–	**2q**	71
18	*p*-$MeO_2CC_6H_4$–	Me–	H–	**2r**	64
19	*p*-$PhCCC_6H_4$–	Me–	H–	**2s**	70
20	*p*-$PhCOC_6H_4$–	Me–	H–	**2t**	73
21	1-Naphthyl–	Me–	H–	**2u**	76
22	Ph–	Et–	H–	**2v**	65

Reaction conditions: tertiary amine (1.0 mmol), NaCN (1.2 mmol), AcOH (6.0 mmol), a 30% aqueous solution of H_2O_2 (2.5 mmol), MCM-41-2N-$RuCl_3$ (5 mol%), MeOH (2 mL) at 60 °C under Ar for 4 h.

[b] Isolated yield.

observed, demonstrating that leached ruthenium species from the catalyst (if any) are not responsible for the observed activity. It was confirmed by ICP-AES analysis that no ruthenium could be detected in the hot filtered solution. The maximum concentration which would have been undetected is 0.06 ppm.

For the practical application of an immobilised transition-metal catalyst, its ease of separation, recoverability and reusability are important factors. This heterogeneous ruthenium catalyst can be easily separated and recovered by a simple filtration of the reaction solution. We next studied recycling of the catalyst by using the oxidative α-cyanation reaction of *N,N*-dimethylaniline (**1j**). After carrying out the reaction, the catalyst was recovered by a simple filtration of the reaction solution and washed with distilled water and ethanol. After being air-dried, it was reused directly without further purification. The recovered ruthenium catalyst was used in the next run and almost consistent activity was observed for eight consecutive cycles (Fig. 1). The satisfactory reusability of the catalyst could be attributed to the chelating action of the bidentate nitrogen ligand on ruthenium and the mesoporous structure of the MCM-41 support. The result is important from industrial and environmental points of view. The high catalytic activity and excellent reusability of the MCM-41-2N-$RuCl_3$ complex make it a highly attractive heterogeneous ruthenium catalyst for the parallel solution phase synthesis of diverse libraries of compounds.

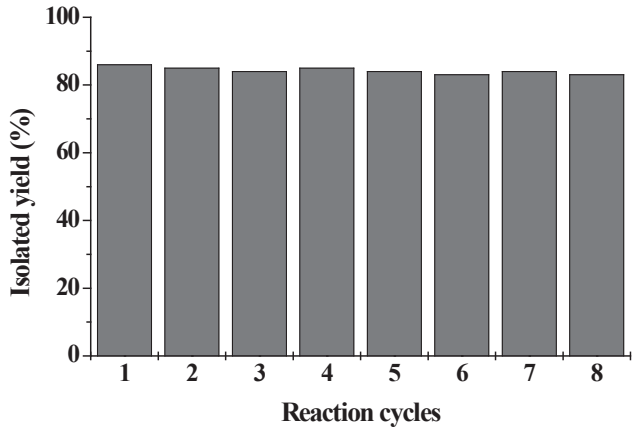


Fig. 1 Recycling of the MCM-41-2N-$RuCl_3$ catalyst.

In summary, we have developed a novel, efficient and cost-effective method for the preparation of α-aminonitriles through oxidative α-cyanation of tertiary amines using an MCM-41-immobilised *N*-alkylethylenediamine ruthenium(III) complex (MCM-41-2N-$RuCl_3$) as the catalyst in the presence of H_2O_2 as oxidant and NaCN in AcOH as the cyanide source. The reactions generated a variety of α-aminonitriles in good yields under mild conditions and were applicable to a range of cyclic or acyclic tertiary amines. In addition, this methodology offers the competitiveness of recyclability of the ruthenium catalyst without significant loss of catalytic activity and the catalyst could be easily recovered and reused at least seven times, thus making this procedure economically and environmentally more acceptable.

Experimental

All chemicals were obtained from commercial suppliers and used as received, unless otherwise noted. All products were characterised by comparison of their spectra and physical data with authentic samples. ^{1}H NMR spectra were recorded on a Bruker Avance 400 spectrometer at 400 MHz with TMS as an internal standard in $CDCl_3$ as solvent. ^{13}C NMR spectra were recorded on the Bruker Avance 400 spectrometer at 100 MHz in $CDCl_3$ as solvent. Microanalyses were measured by using a Yanaco MT-3 CHN microelemental analyser. HRMS spectra were recorded on a Q-Tof spectrometer with micromass MS software using electrospray ionisation (ESI). X-ray diffraction (XRD) measurements were carried out at room temperature using a Philips X'pert diffractometer using Cu Ka radiation filtered by Ni. X-ray energy dispersive spectroscopy (EDS) was performed using a Phenom Prox scanning electron microscope. X-ray photoelectron spectra (XPS) were recorded on an XSAM 800 instrument (Kratos). Mesoporous material MCM-41 was prepared according to a literature method.[37]

Preparation of MCM-41-2N

A solution of 3-(2-aminoethylamino)propyltrimethoxysilane (1.54 g) in dry chloroform (18 mL) was added to a suspension of the MCM-41 (2.2 g) in dry toluene (180 mL). The mixture was stirred for 24 h at 100 °C. The solid was then filtered off and washed with $CHCl_3$ (2 × 20 mL) and dried under reduced pressure at 160 °C for 5 h. The dried white solid was then soaked in a solution of Me_3SiCl (3.1 g) in dry toluene (100 mL) at room temperature under stirring for 24 h. Then the solid was filtered off, washed with acetone (3 × 20 mL) and diethyl ether (3 × 20 mL) and dried under reduced pressure at 120 °C for 5 h to obtain 3.49 g of hybrid material MCM-41-2N. The nitrogen content was found to be 1.84 mmol g^{-1} by elemental analysis.

Preparation of MCM-41-2N-$RuCl_3$ complex

In a small Schlenk tube, MCM-41-2N (2.3 g) was mixed with $RuCl_3 \cdot 3H_2O$ (1.3 mmol, 0.339 g) in dry acetone (50 mL). The mixture

was refluxed for 72 h under an argon atmosphere. The solid product was filtered off by suction, washed with acetone, distilled water and acetone successively and dried at 70 °C/26.7 Pa under Ar for 5 h to give 2.52 g of a grey ruthenium complex (MCM-41-2N-$RuCl_3$). The nitrogen and ruthenium contents were found to be 1.65 mmol g^{-1} and 0.47 mmol g^{-1} respectively.

Heterogeneous Ru-catalysed oxidative α-cyanation of tertiary amines; general procedure

CAUTION: Special precautions should be taken in all procedures involving cyanides due to toxicity. Care should also be taken when heating H_2O_2 or TPHB with organic materials depending on the amounts involved (possible explosion?).

A 25 mL round-bottomed flask equipped with a magnetic stirring bar and a balloon filled with Ar was charged with tertiary amine (1.0 mmol), NaCN (1.2 mmol), acetic acid (6 mmol), MCM-41-2N-$RuCl_3$ (0.05 mmol) and MeOH (2 mL). A 30% H_2O_2 aqueous solution (2.5 mmol) at 60 ºC was added dropwise to the mixture over a period of 1.5 h and the mixture was stirred at 60 ºC for an additional 2.5 h. After completion of the reaction, the mixture was diluted with ethyl acetate (20 mL) and filtered. The catalyst was washed with distilled water (5 mL) and EtOH (2 × 5 mL) and reused in the next run. The filtrate was washed with aqueous $NaHCO_3$ and brine and dried over $MgSO_4$. After removal of the solvent under reduced pressure, the residue was purified by flash column chromatography on silica gel using a mixture of petroleum ether (boiling range 30–60 °C) and EtOAc as eluent.

1-Phenylpyrrolidine-2-carbonitrile (**2a**):[21] Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (t, *J* = 8.0 Hz, 2H), 6.83 (t, *J* = 7.2 Hz, 1H), 6.69 (d, *J* = 8.4 Hz, 2H), 4.43 (dd, *J* = 7.6, 3.6 Hz, 1H), 3.49–3.41 (m, 1H), 3.39–3.33 (m, 1H), 2.44–2.37 (m, 1H), 2.34–2.14 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.3, 129.5, 119.3, 118.3, 112.7, 49.1, 47.5, 31.6, 24.0.

*1-(*o*-Tolyl)pyrrolidine-2-carbonitrile* (**2b**):[22] Brown oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20–7.12 (m, 3H), 7.03 (t, *J* = 7.2 Hz, 1H), 4.38 (dd, *J* = 7.6, 3.6 Hz, 1H), 3.49–3.42 (m, 1H), 3.17–3.12 (m, 1H), 2.42–2.35 (m, 1H), 2.31 (s, 3H), 2.29–1.97 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.9, 132.2, 131.5, 126.8, 124.2, 119.8, 119.1, 52.0, 50.0, 30.7, 22.8, 18.8.

1-(4-Methoxyphenyl)pyrrolidine-2-carbonitrile (**2c**): White solid; m.p. 58–59 ºC (lit.[10] 60–61 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.89 (d, *J* = 9.2 Hz, 2H), 6.66 (d, *J* = 9.2 Hz, 2H), 4.37 (dd, *J* = 7.6, 3.6 Hz, 1H), 3.77 (s, 3H), 3.46–3.40 (m, 1H), 3.15–3.10 (m, 1H), 2.40–2.33 (m, 1H), 2.27–1.96 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.8, 139.9, 119.8, 115.2, 114.1, 55.6, 49.9, 47.8, 31.5, 23.9.

1-Phenylpiperidine-2-carbonitrile (**2d**):[10] Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (t, *J* = 7.2 Hz, 2H), 7.02–6.97 (m, 3H), 4.64–4.61 (m, 1H), 3.47–3.41 (m, 1H), 3.07–2.97 (m, 1H), 2.04–1.99 (m, 2H), 1.86–1.82 (m, 2H), 1.71–1.66 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.8, 129.5, 122.3, 118.5, 117.2, 52.1, 46.6, 29.3, 25.2, 20.2.

1-(4-Methoxyphenyl)piperidine-2-carbonitrile (**2e**): White solid; m.p. 93–94 ºC (lit.[10] 91–93 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.97 (d, *J* = 9.2 Hz, 2H), 6.84 (d, *J* = 9.2 Hz, 2H), 4.47–4.41 (m, 1H), 3.78 (s, 3H), 3.26–3.20 (m, 1H), 3.05–2.99 (m, 1H), 2.03–1.98 (m, 2H), 1.84–1.79 (m, 2H), 1.68–1.63 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.6, 143.9, 120.8, 117.3, 114.6, 55.6, 53.8, 47.9, 29.1, 25.3, 20.2.

1-(2-Nitrophenyl)piperidine-2-carbonitrile (**2f**): Yellow solid; m.p. 55–56 ºC (lit.[22] 56–57 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, *J* = 7.2 Hz, 1H), 7.60 (t, *J* = 7.0 Hz, 1H), 7.48 (d, *J* = 7.6 Hz, 1H), 7.29 (t, *J* = 7.4 Hz, 1H), 4.52–4.49 (m, 1H), 3.38–3.31 (m, 1H), 3.01–2.95 (m, 1H), 2.13–2.07 (m, 1H), 1.99–1.94 (m, 1H), 1.86–1.68 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.5, 144.1, 133.7, 125.6, 125.2, 124.4, 117.1, 54.3, 48.7, 28.9, 25.3, 19.9.

2-Phenyl-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (**2g**):[10] Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (t, *J* = 7.6 Hz, 2H), 7.30–7.21 (m, 4H), 7.08 (d, *J* = 7.6 Hz, 2H), 7.01 (t, *J* = 7.0 Hz, 1H), 5.51 (s, 1H), 3.78–3.72 (m, 1H), 3.51–3.43 (m, 1H), 3.21–3.13 (m, 1H), 2.99–2.93 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.4, 134.7, 129.7, 129.6, 129.4, 128.8, 127.1, 126.9, 121.9, 117.8, 117.6, 53.2, 44.2, 28.6.

2-(3-Methylphenyl)-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (**2h**):[38] Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.18 (m, 5H), 6.89–6.85 (m, 2H), 6.82 (d, *J* = 7.2 Hz, 1H), 5.49 (s, 1H), 3.80–3.69 (m, 1H), 3.48–3.39 (m, 1H), 3.13–3.07 (m, 1H), 2.97–2.89 (m, 1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.5, 139.4, 134.7, 129.8, 129.4, 128.7, 127.1, 126.8, 122.8, 118.4, 117.8, 114.7, 53.3, 44.2, 28.6, 21.7.

2-(4-Bromophenyl)-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (**2i**): Yellow solid; m.p. 155–156 ºC (lit.[38] 153–154 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47–7.41 (m, 2H), 7.34–7.19 (m, 4H), 6.94 (d, *J* = 8.8 Hz, 2H), 5.45 (s, 1H), 3.75–3.64 (m, 1H), 3.52–3.41 (m, 1H), 3.19–3.11 (m, 1H), 3.02–2.89 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.4, 134.4, 132.5, 129.4, 129.3, 128.9, 127.1, 127.0, 119.1, 117.5, 114.4, 52.9, 44.3, 28.4.

2-[Methyl(phenyl)amino]acetonitrile (**2j**):[10] Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (t, *J* = 7.6 Hz, 2H), 6.92 (t, *J* = 7.4 Hz, 1H), 6.87 (d, *J* = 8.4 Hz, 2H), 4.17 (s, 2H), 3.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.4, 129.1, 119.6, 115.4, 114.3, 41.6, 38.7.

*2-[Methyl(*p*-tolyl)amino]acetonitrile* (**2k**):[10] Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.12 (d, *J* = 8.0 Hz, 2H), 6.80 (d, *J* = 8.4 Hz, 2H), 4.13 (s, 2H), 2.96 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.3, 129.5, 129.4, 127.5, 115.0, 42.4, 39.0, 19.9.

*2-[Methyl(*m*-tolyl)amino]acetonitrile* (**2l**):[11] Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27–7.11 (m, 1H), 6.74 (d, *J* = 7.6 Hz, 1H), 6.70–6.66 (m, 2H), 4.14 (s, 2H), 2.98 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.4, 138.8, 128.8, 124.4, 120.6, 115.2, 111.6, 41.8, 38.8, 21.3.

2-[(4-Bromophenyl)methylamino]acetonitrile (**2m**):[10] Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (dd, *J* = 7.2, 2.0 Hz, 2H), 6.73 (dd, *J* = 8.8, 2.0 Hz, 2H), 4.14 (s, 2H), 2.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.3, 131.8, 115.9, 114.7, 112.0, 41.7, 38.9.

2-[(3-Chlorophenyl)methylamino]acetonitrile (**2n**):[22] Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.18–7.12 (m, 1H), 6.80 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.74 (t, *J* = 2.2 Hz, 1H), 6.64 (dd, *J* = 8.4, 2.8 Hz, 1H), 4.08 (s, 2H), 2.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.8, 134.3, 129.4, 118.9, 114.2, 113.7, 111.6, 40.9, 38.1.

4-[(Cyanomethyl)methylamino]benzonitrile (**2o**): Yellow solid; m.p. 105–106 ºC (lit.[14] 106–107 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, *J* = 8.4 Hz, 2H), 6.82 (d, *J* = 8.8 Hz, 2H), 4.26 (s, 2H), 3.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.8, 144.4, 133.3, 117.7, 114.0, 112.9, 40.5, 38.5.

2-[Biphenyl-4-yl(methyl)amino]acetonitrile (**2p**): White solid; m.p. 103–104 ºC; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57–7.52 (m, 4H), 7.41 (t, *J* = 7.8 Hz, 2H), 7.32–7.28 (m, 1H), 6.92 (d, *J* = 8.8 Hz, 2H), 4.18 (s, 2H), 3.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.1, 140.6, 133.0, 128.8, 128.1, 126.7, 126.6, 115.5, 115.1, 42.2, 39.3; HRMS (ESI) *m/z* calcd for $C_{15}H_{14}N_2^+$ [M^+]: 222.1157; found: 222.1164.

2-[(4'-Fluorobiphenyl-4-yl)(methyl)amino]acetonitrile (**2q**): White solid; m.p. 121–123 ºC; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51–7.46 (m, 4H), 7.12–7.06 (m, 2H), 6.91 (d, *J* = 8.8 Hz, 2H), 4.19 (s, 2H), 3.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.1 (d, $^1J_{C-F}$ = 244.1 Hz), 147.0, 136.7 (d, $^4J_{C-F}$ = 3.2 Hz), 132.1, 128.1 (d, $^3J_{C-F}$ = 7.9 Hz), 128.0, 115.6 (d, $^2J_{C-F}$ = 21.2 Hz), 115.4, 115.1, 42.2, 39.3; HRMS (ESI) *m/z* calcd for $C_{15}H_{13}FN_2^+$ [M^+]: 240.1063; found: 240.1051.

Methyl 4-[(cyanomethyl)methylamino]benzoate (**2r**): White solid; m.p. 80–81 ºC (lit.[22] 81–82 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (dd, *J* = 7.2, 2.0 Hz, 2H), 6.80 (dd, *J* = 7.2, 2.0 Hz, 2H), 4.25 (s, 2H), 3.88 (s, 3H), 3.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.9, 150.9, 131.5, 120.8, 115.2, 112.8, 51.8, 41.2, 39.0.

2-{Methyl[4-(phenylethynyl)phenyl]amino}acetonitrile (**2s**): Yellow solid; m.p. 107–109 ºC; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53–7.44 (m, 4H), 7.36–7.28 (m, 3H), 6.78 (dd, *J* = 7.2, 2.0 Hz, 2H), 4.15 (s, 2H), 3.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.4, 133.0, 131.5, 128.4, 128.0, 123.7, 115.3, 114.2, 114.1, 89.5, 88.4, 41.7, 39.1. HRMS (ESI) *m/z* calcd for $C_{17}H_{14}N_2^+$ [M^+]: 246.1157; found: 246.1162.

2-[(4-Benzoylphenyl)methylamino]acetonitrile (**2t**): Yellow solid; m.p. 94–95 ºC (lit.[39] 92–93 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84

(d, *J* = 8.8 Hz, 2H), 7.77–7.72 (m, 2H), 7.55 (t, *J* = 7.2 Hz, 1H), 7.47 (t, *J* = 7.4 Hz, 2H), 6.84 (d, *J* = 9.2 Hz, 2H), 4.29 (s, 2H), 3.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.3, 150.8, 138.4, 132.7, 132.6, 129.7, 128.3, 128.2, 115.1, 112.6, 41.2, 39.1.

2-[Methyl(naphthalen-1-yl)amino]acetonitrile (**2u**): Yellow solid; m.p. 91–93 ºC (lit.[39] 91–92 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (d, *J* = 8.4 Hz, 1H), 7.86 (d, *J* = 7.2 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.55–7.47 (m, 2H), 7.44 (t, *J* = 7.8 Hz, 1H), 7.33 (d, *J* = 7.6 Hz, 1H), 4.10 (s, 2H), 3.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.6, 128.2, 127.5, 125.7, 125.5, 125.2, 124.9, 124.6, 122.2, 117.0, 116.7, 45.6, 40.9.

2-[Ethyl(phenyl)amino]acetonitrile (**2v**):[17] Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (t, *J* = 8.0 Hz, 2H), 6.92 (t, *J* = 7.2 Hz, 1H), 6.86 (d, *J* = 8.0 Hz, 2H), 4.14 (s, 2H), 3.44 (q, *J* = 7.2 Hz, 2H), 1.24 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.4, 129.1, 119.3, 115.9, 114.5, 45.8, 39.0, 11.8.

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Electronic Supplementary Information

The ESI (details of XRD, EDS and XPS characterisation data for the MCM-41-2N-$RuCl_3$ complex) is available through http://ingentaconnect.com/content/stl/jcr/2017/00000041/00000010

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