Sustainable Alkylation of Nitriles with Alcohols by Manganese Catalysis

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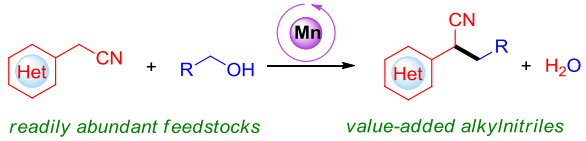
ABSTRACT: A general and chemoselective catalytic alkylation of nitriles using a homogenous non-precious manganese catalyst is presented. This alkylation reaction uses naturally abundant alcohols and readily available nitriles as coupling partners. The reaction tolerates a wide range of functional groups and heterocyclic moieties, efficiently providing useful cyanoalkylated products with water as the only side product. Importantly, methanol can be used as a C1 source and the chemoselective *C*-methylation of nitriles is achieved. The mechanistic investigations support the multiple role of the metal-ligand manganese catalyst; the dehydrogenative activation of the alcohol; α-C-H activation of the nitrile; and hydrogenation of the *in-situ* formed unsaturated intermediate.

INTRODUCTION

The construction of C−C bonds via the hydrogen autotransfer strategy is of particular academic and industrial interest. The key motivation for this strategy is the application of alcohol feedstock as a benign alkylating reagent,[1] while liberating water as the sole by-product. Thus, the procedure eliminates the need for mutagenic alkyl halides and avoids the production of copious waste. To date the majority of appropriate catalytic systems are based on noble metals including Ru, Rh, Ir, Pd and Pt.[2] The low availability of these precious metals has triggered the development of alternative catalytic systems based on earth abundant metals.[3] In this context, progress has been made in the alkylation of ketones,[4] alcohols,[5] esters,[6] and amides [6] using base metal catalysts. In contrast, the alkylation of nitriles is more challenging due to the sensitivity of the cyano group towards the activated hydrogen and the water side product. In more detail, the metal catalyst can transfer hydrogen from the alcohol to the nitriles to form primary amines and aldehydes,[7] and these can subsequently be converted to secondary amines[8] or amides.[9] However, water might result in the hydrolysis of the nitrile functionality to the corresponding amide.[10] In addition, the alkylation of nitriles with alcohols often leads to a mixture of the alkylnitrile product along with the corresponding olefin intermediate,[11] giving rise to critical selectivity issues. Thus, until recently, the direct alkylation of nitriles with alcohols was only known with precious metal catalysis such as Ru,[12] Ir,[13] Rh,[14] Os[15] and Pd.[16]

Our interest in the development of an improved synthesis of alkylnitriles is due to their great importance as valuable intermediates in the fine chemical industry. Importantly, the cyanoalkyl moiety is also ubiquitous in different natural products and pharmaceuticals.[17] Very recently, Wang and coworkers have reported an interesting iron catalysed alkylation of nitriles with primary alcohols, by applying stoichiometric amount of strong base (NaOH).[18] Pursuant to our interest in developing sustainable transformations based on nonprecious metal catalysis,[19] and inspired by the recent advances in manganese catalysis,[20-22] we herein report highly reactive and selective manganese catalysed alkylation of non-activated nitriles with a broad range of alcohols (Scheme 1). A related study has also been reported by Maji et. al.[23] In our study we focused on a catalytic system that utilizes a bench stable catalyst which can easily be prepared in one step from the commercially available and air stable MACHO ligand and $Mn(CO)_5Br$. Interestingly, the presented catalytic system is not limited to the long-chain alcohols as the more challenging *C*-alkylation can also be achieved with methanol as C1-source. Furthermore, the manganese catalyst does not require any sensitive reagents for activation and is simply activated with catalytic amounts of suitable base.

Scheme 1. Manganese Catalyzed Alkylation of Nitriles with Alcohols

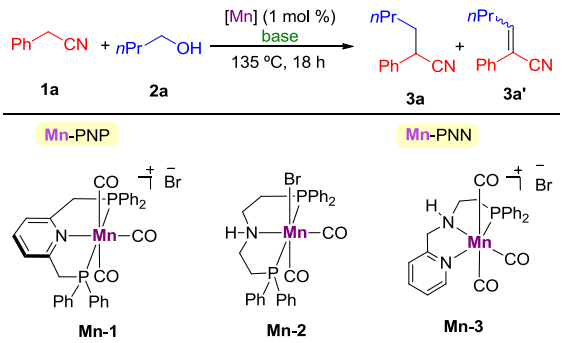


RESULTS AND DISCUSSION

In order to develop the base metal catalyzed alkylation reaction we started to investigate the reaction between phenylacetonitrile (**1a**) and the *n*-butanol (**2a**) applying different manganese catalysts (Table 1). Initially, we screened the catalytic activity of the different manganese complexes **Mn-1** to **Mn-3** in toluene using *t*-BuOK as the catalyst activator. The pyridyl-based PNP complex **Mn-1**[22j] led to unsatisfactory results providing only a trace amount of the product (Table 1, entry 1). However, in the presence of the complex **Mn-2**,[22k] bearing an aliphatic NH group, excellent conversion was observed and 86% of the desired product **3a** along with 11 % of the unsaturated olefin **3a**'(Table 1, entry 2) was obtained. Use of the Mn-PNN pincer complex **Mn-3**[20b] (Table 1, entry 3) provided similar results. Due to the facile access of **Mn-2** and the availability of the ligand, we decided to further optimize the model reaction using **Mn-2** in combination with different bases and solvents. Running the reaction using equimolar amounts of the manganese and the base, resulted in 66% con-

version and 47% combined yield of **3a** and **3a'** (Table 1, entry 4). Using polar solvents such as *t*-amyl alcohol, 1,4-Dioxane or 2-Me-THF, did not lead to improved results (Table 1, entries 5-7). In addition, we tested various bases including KOH, K_2CO_3 and Cs_2CO_3 (Table 1, entries 8-10). From these experiments the best results were obtained using Cs_2CO_3 and the desired product was obtained in 79% yield along with 8% of the alkenyl nitrile **3a'**. Pleasingly, slightly increasing the base loading to 10 mol % led to quantitative yield with complete chemoselectivity (Table 1, entry 11).

Table 1. Optimization of the Reaction Conditions.[a]



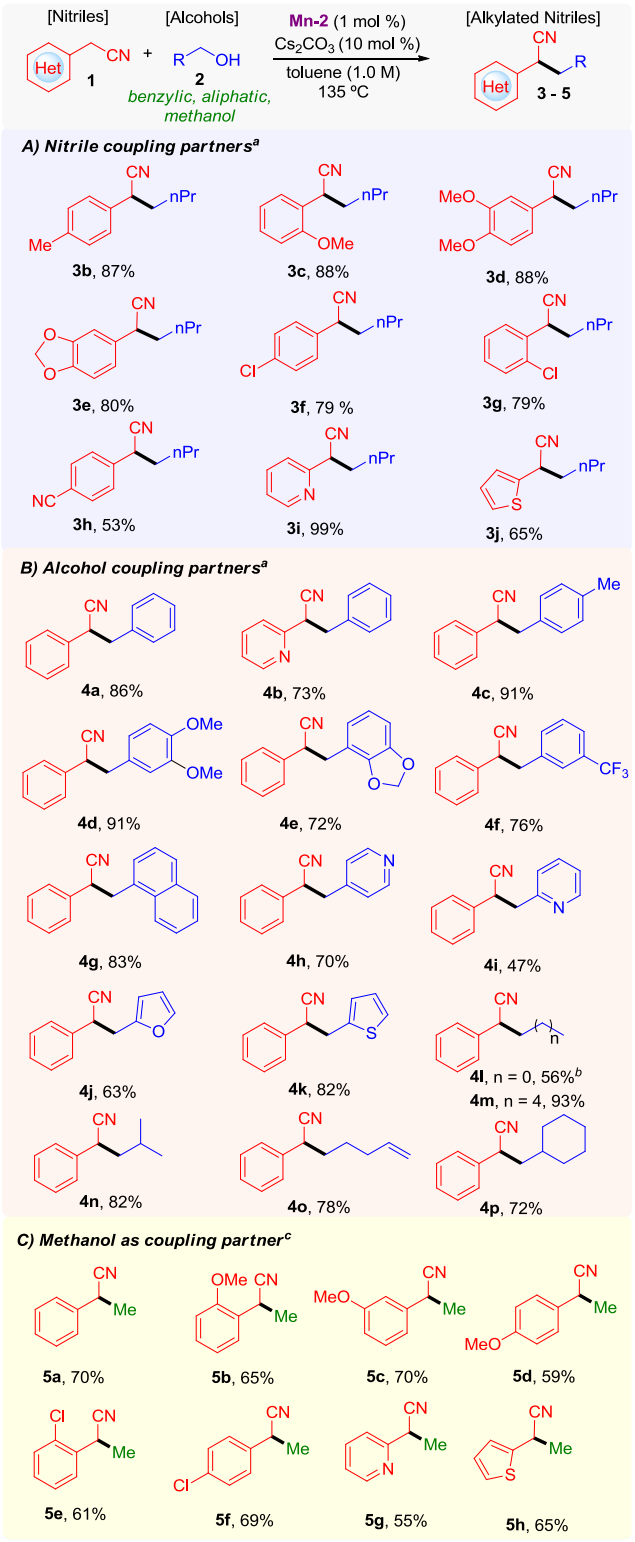
entry	cat.	base (mol %)	conv. (%)	yield **3a**/**3a'**(%)
1	**Mn-1**	*t*-BuOK (3)	38	>5/>5
2	**Mn-2**	*t*-BuOK (3)	97	86/11
3	**Mn-3**	*t*-BuOK (3)	96	70/09
4	**Mn-2**	*t*-BuOK (1)	66	35/12
5[b]	**Mn-2**	*t*-BuOK (3)	95	77/12
6[c]	**Mn-2**	*t*-BuOK (3)	48	25/06
7[d]	**Mn-2**	*t*-BuOK (3)	78	60/10
8	**Mn-2**	KOH (3)	>99	96/04
9	**Mn-2**	K_2CO_3 (3)	84	67/12
10	**Mn-2**	Cs_2CO_3 (3)	>99	79/08
11	**Mn-2**	Cs_2CO_3 (10)	>99	99/00

[a]Reaction conditions: **1a** (0.5 mmol), **2a** (1 mmol), [**Mn**] (0.005 mmol) and base in toluene (0.5 mL) at 135 °C in a glass tube under an inert atmosphere for 18 h. Conversions and yields were determined by GC analysis of the crude reaction mixture using mesytilene as an internal standard. [b]Reaction in *t*-amyl alcohol. [c]Reaction in 2-Me THF. [d]Reaction in 1,4-dioxane.

Having established the optimized reaction conditions, we next investigated the generality of this protocol by exploring the scope of the nitrile alkylation partner (Scheme 2A). To our delight, in all cases the reaction was accomplished within 18 h using 1 mol % of the bench stable catalyst **Mn-2**. Notably, a diverse range of substituted benzyl cyanides can be used to yield the *C*-alkylated nitriles derivatives **3b** – **3g** in very good yields and with excellent chemoselectivity. It is important to highlight that the benzonitrile moiety was tolerated to give the desired product **3h**. Importantly, heterocycle containing benzylic nitriles, such as **3i** and **3j** can also be efficiently alkylated.

We next decided to explore the scope of primary alcohols as alkylating agents (Scheme 2B). Importantly, a large array of benzyl alcohols bearing electron withdrawing and electron donating groups in different positions could be applied to give

Scheme 2. Manganese Catalyzed Alkylation of Nitriles with Different Alcohols.



[a] Reaction conditions: **1** (0.5 mmol), **2** (1 mmol), **Mn-2** (0.005 mmol), Cs_2CO_3 (0.05 mmol), toluene (0.5 mL), 135 °C (aluminum block), 18 h. [b]**Mn-2** (0.025 mmol). [c]Reaction conditions: **1** (0.5 mmol), methanol (1 mL), **Mn-2** (0.025 mmol), Cs_2CO_3 (0.05 mmol), 1,4-dioxane (1 mL), 24 h.

the desired products **4a**-**4f** in very good isolated yields. Furthermore, a naphthyl-substituted product **4g** was obtained in 83% yield. Similar to the scope of the nitrile, alcohols bearing heterocyles (pyridine, thiophene, furane) could also be used to access the corresponding products **4h**-**4k**. Moreover, this protocol is not limited to benzlic alcohols, as exemplified by the rapid incorporation of different aliphatic alcohols under the same reaction conditions (**4l**-**4p**), whereby unsaturated C=C bonds remain intact (**4o**).

However, a higher activation energy barrier needs to be overcome for the dehydrogenation of the methanol compared with other alcohols, our catalytic system proved to be suitable for the challenging α-methylation of nitriles. Slightly modified reaction conditions have to be used to successfully accomplish the C1-alkylation. Indeed, a broad series of differently substituted nitriles, including heterocycles, can be methylated to deliver the products **5a**–**5h** in moderate to good yields (Scheme 2C). Interestingly, our base metal catalyzed procedure shows superior catalytic activity to the recently disclosed Ru-catalyzed protocol.[12a]

In order to gain more insight into the reaction mechanism we monitored the reaction progress between phenylacetonitrile (**1a**) and 1-butanol (**2a**) catalyzed by **Mn-2** (Figure 1). After 1 hour, we observed 83% of conversion of the nitrile **1a** and the formation of 66% yield of **3a** along with 15% of the unsaturated intermediate **3a'**. After 3 hours, almost full conversion of **1a** was obtained with 80% yield of the **3a**, while the amount of the remaining intermediate **3a'** was still constant (ca.15 %). Complete conversion was observed after 18 hours. Subsequently, we decided to carry out several control NMR experiments (Figure 2). The treatment of **Mn-2** with one equivalent of *t*-BuOK at room temperature for one hour in C_6D_6 led to the formation of the soluble imido complex **Mn-2a** as confirmed by the ^{31}P-NMR spectrum (91.02 ppm). When one equivalent of 4-flurophenylacetonitrile was added, we immediately observed the formation of two new broad peaks at 73.65 and 78.82 ppm at ^{31}P-NMR, indicating the coordination between the manganese catalyst and the nitrile substrate.

Based on the experimental background and the DFT studies, a proposed reaction mechanism is shown in Scheme 3. Initially, the manganese pre-catalyst reacts with the base to generate an imido complex as the active catalytic species (Scheme 3a). This imido complex activates the alcohol via dehydrogenation with the simultaneous formation of the manganese species H-Mn-N-H. Most likely, this reaction takes place via the formation of a Mn-alkoxide intermediate. In addition to the role of the manganese catalyst in the alcohol activation, the NMR experiment indicates the role of the metal catalyst in the C-H activation of the nitrile substrate. [24] The two new broad peaks in figure **2c** most likely correlate to the species **A** and **B** in scheme 3b. The initial coordination of the nitrile substrate with the 16e species lead to the formation of the molecule **A**. Then, the ligand plays a crucial role for the hydrogen abstraction and the generation of the highly nucleophilic species **B**.[25] Thus, the same metal catalyst simultaneously activates both of the substrates to produce the electrophile (aldehyde) and nucleophile **B**. the addition of the intermediate **B** to the in-situ generated aldehyde delivers the intermediate **C** and one molecule of water. This intermediate leads to the formation of the olefin intermediate **3'** and regenerates the **Mn-2a**. Finally, the shuttled hydrogen on the H-Mn-N-H is transferred to **3'** to produce the α-alkylated nitrile **3** via a metal-ligand cooperative mechanism.

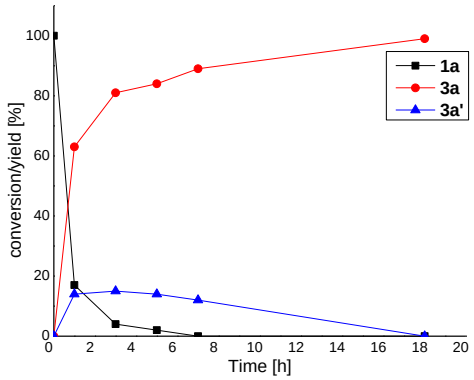


Figure 1. Monitoring of the reaction progress (reaction conditions as in table 1, entry 11).

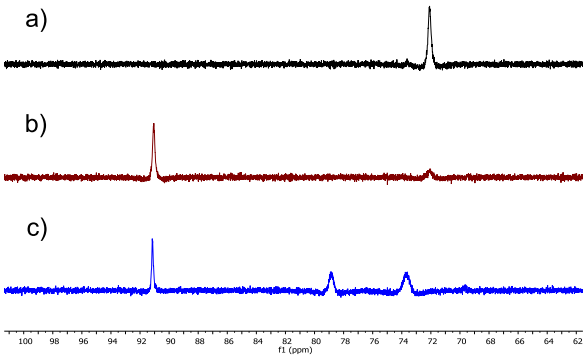
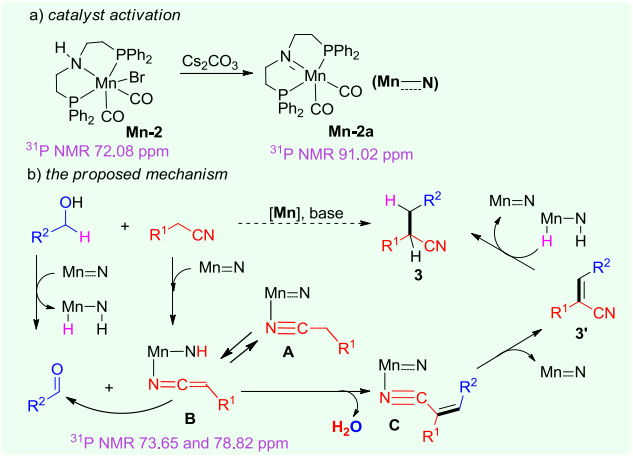


Figure 2. ^{31}P NMR spectra at RT. a) **Mn-2** in CD_2Cl_2. b) **Mn-2** + 1 equiv. *t*-BuOK in C_6D_6. c) **Mn-2** + 1 equiv. of *t*-BuOK+1 equiv. of 4-flurophenylacetonitrile in C_6D_6.

Scheme 3. Proposed Reaction Mechanism



CONCLUSION

In summary, manganese PNP pincer catalyzed alkylation of nitriles with alcohols is reported. This environmentally benign, hydrogen autotransfer reaction is characterized by the absence of noble metals and stoichiometric reagents, generating water as the only side product. A broad range of alcohols could be

used as green alkylating reagents and, importantly, the challenging methylation reaction is feasible, resulting in the desired C-methylated nitriles with excellent chemo-selectivity. The experimental studies support the reaction mechanism in which the manganese catalyst plays a multiple role in activating both the reaction partners as well as the subsequent hydrogenation of the alkenyl nitrile to selectively produce the highly value-added α-alkylated nitriles.

EXPERIMENTAL SECTION

General Method

All reactions were carried out under an argon atmosphere using oven-dried glassware. Purified compounds were further dried under high vacuum (0.01–0.05 Torr). Yields refer to purified compounds. Analytical thin-layer chromatography (TLC) was performed using silica gel 60 pre-coated aluminium plates (Macherey-Nagel 0.20 mm thickness) with a fluorescent indicator UV254. Visualization was performed with standard phosphomolybdic acid stain (10g in 100 mL EtOH) or UV light. Column chromatography was performed using Macherey-Nagel Aluminium oxide 90 neutral (50–200 µm). ^{1}H-NMR, ^{13}C-NMR and ^{31}P-NMR spectra were recorded on VNMRS-400, VNMRS-600 or Mercury 300 spectrometer in $CDCl_3$. Chemical shifts (δ) are reported in ppm and multiplicities are indicated: s (singlet), d (doublet), dd (doublet of doublet, t (triplet), dt (doublet of triplet), td (triplet of doublet), q, (quartet), quint (quintet) m (multiplet); coupling constants (J) are in Hertz (Hz). The abbreviation "vt" corresponds to a "virtual triplet" due to scalar coupling with two magnetically nonequivalent phosphorus nuclei. Mass spectra were acquired on a Finnigan SSQ7000 (EI/CI) spectrometer and high resolution mass spectra on a Finnigan MAT 95 (EI/CI) or on a ThermoFisher Scientific LTQOrbitrap XL (ESI) using ion trap as analyzer type. IR spectra were recorded on a Perkin Elmer Spectrum 100 spectrometer and are reported in terms of frequency of absorption (cm^{-1}).

Synthesis of tricarbonyl(2,6-bis((diphenylphosphaneyl)methyl)pyridine)manganese(I) bromide (Mn-1).[22j]

A flame dried Schlenk tube was charged with $Mn(CO)_5Br$ (420 mg, 1.53 mmol, 1.0 eq.) and the pincer PNP ligand (800 mg, 1.68 mmol, 1.1 eq.). The tube was evacuated and backfilled with argon for three times. THF (25 mL) was added and the resulting orange suspension was heated to 60 °C (oil bath) and stirred for 20 h. The solution was allowed to cool to room temperature and THF was removed *in vacuo*. The work-up was done under ambient atmosphere. The yellow solid was washed three times with *n*-hexane (3 x 5 mL). The crude yellow powder was taken into dichloromethane and transferred into a 50 mL round bottom flask to remove insoluble inorganic side products. The solution was concentrated under reduced pressure and the complex **Mn-1** was isolated as a yellow powder (1.02 g, 95%); ^{1}H NMR (300 MHz, CD_2Cl_2) δ 8.09 (s, 2H), 7.81 – 7.26 (m, 21H), 4.65 (s, 4H); ^{31}P{^{1}H} NMR (243 MHz, CD_2Cl_2) δ 69.4. (s, 2P); IR (ATR) 1918, 1840, 1571, 1435, 1284, 1172, 1097, 964, 833, 696 cm^{-1}; HRMS (ESI+): *m/z* $[M - Br]^+$ calcd for $C_{34}H_{27}MnNO_3P_2$, 614.0841; found, 614.0853.

Synthesis of bromodicarbonyl(bis(2-(diphenylphosphaneyl)ethyl)amine)manganese(I) (Mn-2).[22K]

A flame dried Schlenk tube was charged with the HCl salt of the PNP pincer ligand (478 mg, 1.0 mmol, 1.0 equiv.), toluene (8 mL), water (2 mL) and NaOH (120 mg, 3.0 mmol, 3.0 equiv.). The reaction mixture was stirred at 45 °C (oil bath) for 30 min. The two phases were separated, and the organic layer was washed with water (5 × 5 mL). The pH-value was checked until the solution turned neutral. The organic layer was concentrated under reduced pressure. Subsequently, toluene (12 mL) and $Mn(CO)_5Br$ precursor were added to the Schlenk tube. The reaction mixture was heated up to 110 °C (oil bath) and the atmosphere was exchanged three times by evacuating and backfilled with argon. After the mixture was stirred for 20 h at reflux temperature, it was cooled to room temperature and concentrated *in vacuo*. The crude precipitate was washed with pentane and extracted with dichloromethane/diethylether to remove insoluble inorganic side products. The solution was concentrated under reduced pressure and dried to afford the complex **Mn-2** as a yellow powder (410 mg, 65%). ^{1}H NMR (600 MHz, CD_2Cl_2) δ 7.92 – 7.89 (m, 4H, CH_{Ar}), 7.60 – 7.57 (m, 4H, CH_{Ar}), 7.43 – 7.29 (m, 12H, CH_{Ar}), 3.74 – 3.59 (m, 2H, NCH_2CH$_2$), 3.52 (br, 1H, N*H*), 3.32 – 3.23 (m, 2H, NCH_2CH$_2$), 2.78 – 2.73 (m, 2H, NCH$_2$CH_2), 2.44 – 2.40 (m, 2H, NCH$_2$CH_2); ^{31}P{^{1}H} NMR (243 MHz, CD_2Cl_2) δ = 69.7 (s); ^{13}C{^{1}H} NMR (151 MHz, CD_2Cl_2) δ =231.6 (br, CO), 226.0 (br, CO), 137.9 (vt, *J* = 19.1 Hz, P$C_{Ar,ipso}$), 135.5 (vt, *J* = 19.1 Hz, P$C_{Ar,\ ipso}$), 133.8 (vt, *J* = 5.0 Hz, CH_{Ar}), 130.6 (vt, *J* = 5.0 Hz, CH_{Ar}), 130.3 (s, CH_{Ar}), 129.6 (s, CH_{Ar}), 129.0 (vt, *J* = 4.3 Hz, CH_{Ar}), 128.7 (vt, *J* = 4.6 Hz, CH_{Ar}), 53.0 (vt, *J* = 4.7 Hz, NCH_2CH$_2$), 28.4 (vt, *J* = 8.9 Hz, NCH$_2$CH_2); IR (ATR): ν^{-1} 3189, 1910, 1826 cm^{-1}; HRMS (ESI+): *m/z* $[M - Br]^+$: calcd for $C_{30}H_{29}MnNO_2P_2$, 552.1049; found, 552.1050.

Synthesis of dicarbonyl(bis(2-(diphenylphosphaneyl)ethyl)amide)-manganese(I) (Mn-2a).

In an argon filled glovebox complex **Mn-2** (127 mg, 0.2 mmol) was introduced into a 25 mL Schlenk tube and was dissolved in toluene (5 mL). After 2 min stirring, *t*-BuOK (34 mg, 0.3 mmol) was added upon which the yellow solution turned deep red. The reaction mixture was stirred for 1h at 50 °C (oil bath). Then the mixture was filtered and the solution was concentrated under reduced pressure to give a deep red powder (75 mg, 68%) that was stored in glovebox. ^{1}H NMR (600 MHz, C_6D_6) δ 7.73 – 7.71 (m, 8H, CH_{Ar}), 7.10 – 7.08 (m, 8H, CH_{Ar}), 7.04 – 7.02 (m, 4H), 3.25 – 3.24 (m, 4H, NCH_2CH$_2$), 2.35 – 2.32 (m, 4H, NCH$_2$CH_2); ^{31}P{^{1}H} NMR (243 MHz, C_6D_6) δ 91.06 (s); ^{13}C{^{1}H} NMR (151 MHz, C_6D_6) δ = 233.5 (br, CO), 136.6 (vt, *J* = 18.0 Hz, P$C_{Ar,ipso}$), 132.7 (s, CH_{Ar}), 129.8 (s, CH_{Ar}), 128.8 (vt, *J* = 4.3 Hz, CH_{Ar}), 62.1 (NCH_2CH$_2$), 33.7 (NCH$_2$CH_2); IR (ATR): 1903, 1828 cm^{-1}, (no ν_{NH} band observed).

Synthesis of tricarbonyl(2-(diphenylphosphaneyl)-N-(pyridin-2-ylmethyl)ethan-1-amine)manganese(I) bromide (Mn-3).[206]

A flame dried Schlenk tube was charged with the PNN pincer ligand (300 mg, 1.07 mmol, 1 eq.) and $Mn(CO)_5Br$ (293 mg, 1.07 mmol, 1.0 eq.). The Schlenk tube was evacuated and backfilled with argon for several time. Afterwards, 15 mL of degassed THF was added and the reaction mixture was stirred at 80 °C (oil bath) for 20 h. The suspension was allowed to cool to room temperature and the yellow precipitate was filtered off and washed with diethyl ether and n-hexane. The remaining solid was dried under vacuum to afford the complex **Mn-3** as a yellow powder (0.49 g, 84%); ^{1}H NMR (600 MHz, DMSO-*d6*): δ 7.93 – 7.92 (m, 1H), 7.87 – 7.84 (m, 2H), 7.81-7.78 (m, 1H), 7.58-7.49 (m, 4H), 7.39 – 7.37 (m, 1H), 7.31 – 7.29 (m, 2H), 7.20 – 7.09 (m, 2H), 6.94 – 6.92 (m, 1H), 4.58 – 4.54 (m, 1H), 4.38 (m, 1H), 3.28 – 3.20 (m, 1H), 3.04 – 3.00 (m, 1H), 2.95-2.89 (m, 1H), 2.40 – 2.27 (m, 1H); ^{13}C{^{1}H} NMR (151 MHz, DMSO-*d6*) δ 221.2, 219.9, 215.3, 162.1, 153.0, 139.2, 132.4, 132.0, 131.1, 131.0, 130.9, 130.8, 129.9, 129.8, 129.6, 125.0, 122.4, 59.8, 53.8 (d, *J* = 8.8 Hz), 22.7 (d, *J* = 22.7 Hz); ^{31}P{^{1}H} NMR (242 MHz, DMSO-*d6*) δ 65.86; IR (ATR): 3045, 2891, 2024, 1914, 1843, 1477, 1434, 1099, 892, 752, 693 cm^{-1}; HRMS (ESI): *m/z* $[M\text{-}Br]^+$ calcd for $C_{23}H_{21}MnN_2O_3P$, 459.0665; found, 459.0675.

General procedure of *C*-alkylation of nitriles using aliphatic and benzylic alcohols

A glass pressure tube (10 mL) equipped with a magnetic stirrer was charged with **Mn-2** (3.2 mg, 0.005 mmol), Cs_2CO_3 (16.3 mg, 0.05 mmol). A rubber septum was attached to the tube and the reaction vessel was evacuated and backfilled with argon for three times. Under an inert atmosphere primary alcohol (1.0 mmol), nitrile (0.5 mmol) and toluene (0.5 mL) were added and the tube was closed with a screw cap. The resulting mixture was stirred at 135 °C (aluminum block) for 18 h under argon atmosphere. Upon cooling down to room temperature the residue was directly purified by flash column chromatography on silica gel eluting with pentane: diethyl ether (20:1 (v/v)) to give the pure alkylated nitrile.

*2-phenylhexanenitrile (**3a**).*[12a] Colorless oil; 78 mg (88%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.27 (m, 5H), 3.77 (dd, *J* = 8.5, 6.3 Hz,

1H), 2.04 – 1.74 (m, 2H), 1.60 – 1.25 (m, 4H), 0.92 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 136.2, 129.1, 128.0, 127.3, 121.0, 37.5, 35.7, 29.2, 22.2, 13.8.

*2-(p-tolyl)hexanenitrile (**3b**)*[13d] Colorless oil; 81 mg (87%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25 – 7.16 (m, 4H), 3.74 (dd, *J* = 8.6, 6.3 Hz, 1H), 2.36 (s, 3H), 1.99 – 1.77 (m, 2H), 1.55 – 1.29 (m, 4H), 0.92 (t, *J* = 7.3 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 137.8, 133.1, 129.7, 127.2, 121.2, 37.0, 35.7, 29.2, 22.2, 21.1, 13.9.

*2-(2-methoxyphenyl)hexanenitrile (**3c**).*[12a] Colorless oil; 96 mg (94%); eluent mixture: pentane: diethyl ether (10:1 (v/v)), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.40 (m, 1H), 7.30 – 7.27 (m, 1H), 7.00 – 6.96 (m, 1H), 6.91 – 6.82 (m, 1H), 4.19 (dd, *J* = 8.2, 6.3 Hz, 1H), 3.85 (s, 3H), 1.86 (m, 2H), 1.62 – 1.23 (m, 4H), 0.92 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 156.1, 129.3, 128.3, 124.5, 121.4, 120.9, 110.8, 55.5, 33.5, 31.4, 29.4, 22.1, 13.8.

*2-(3,4-dimethoxyphenyl)hexanenitrile (**3d**).* Colorless oil; 103 mg (88%); eluent mixture: pentane: diethyl ether (5:1 (v/v)); ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.85 – 6.76 (m, 3H), 3.86 (s, 3H), 3.84 (s, 3H), 3.68 (dd, *J* = 8.7, 6.3 Hz, 1H), 1.94 – 1.75 (m, 2H), 1.50 – 1.26 (m, 4H), 0.87 (t, *J* = 7.3 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 149.3, 148.7, 128.4, 121.2, 119.5, 111.3, 110.2, 110.1, 56.0, 55.9, 36.9, 35.6, 29.1, 22.1, 13.8; IR: 2936, 2865, 2087, 1906, 1595, 1457, 1343, 1253, 1146, 1026, 913, 809, 759 cm^{-1}. HRMS (ESI+): *m/z* $[M]^+$ calcd for $C_{14}H_{19}O_2N$, 233.1410; found 233.1413.

*2-(benzo[d][1,3]dioxol-5-yl)hexanenitrile (**3e**).*[12a] Colorless oil; 87 mg (80%); eluent mixture: pentane: diethyl ether (5:1 (v/v)); ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.81 – 6.73 (m, 3H), 5.96 (s, 2H), 3.67 (dd, *J* = 8.5, 6.4 Hz, 1H), 1.93 – 1.74 (m, 2H), 1.50 – 1.27 (m, 4H), 0.94 – 0.85 (m, 3H); $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 148.2, 147.4, 129.8, 121.1, 120.7, 108.6, 107.7, 107.7, 101.4, 37.1, 35.7, 29.1, 22.1, 13.8.

*2-(4-chlorophenyl)hexanenitrile (**3f**).*[26a] Colorless oil; 82 mg (79%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 – 7.25 (m, 4H), 3.75 (dd, *J* = 8.6, 6.2 Hz, 1H), 1.97 – 1.77 (m, 2H), 1.51 – 1.28 (m, 4H), 0.90 (t, *J* = 7.3 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 134.6, 134.0, 129.3, 128.7, 120.6, 36.9, 35.6, 29.1, 22.1, 13.8.

*2-(2-chlorophenyl)hexanenitrile (**3g**).* Colorless oil; 82 mg (79%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56 – 7.55 (m, 1H), 7.42 – 7.36 (m, 1H), 7.32 – 7,31 (m, 1H), 7.28 – 7.25 (m, 1H), 4.28 (dd, *J* = 9.0, 5.6 Hz, 1H), 1.96 – 1.79 (m, 2H), 1.61 – 1.30 (m, 4H), 0.92 (t, *J* = 7.4 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 134.0, 132.6, 130.0, 129.5, 128.9, 127.7, 120.5, 34.7, 34.0, 29.3, 22.1, 13.9; IR: 3424, 2935, 2866, 2666, 2323, 2103, 1921, 1728, 1466, 1278, 1040, 754 cm^{-1}; HRMS (ESI+): *m/z* $[M + Na]^+$ calcd for $C_{12}H_{14}N_1Cl_1Na_1$ 230.0707; found, 230.0707.

*4-(1-cyanopentyl)benzonitrile (**3h**).* Yellowish oil; 52 mg (53%)*;* ^{1}H NMR (600 MHz, CDCl3) δ 7.70 – 7.68 (m, 2H), 7.47 – 7.46 (m, 2H), 3.85 (dd, *J* = 8.6, 6.1 Hz, 1H), 1.98 – 1.82 (m, 2H), 1.54 – 1.29 (m, 4H), 0.91 (t, *J* = 7.3 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 141.3, 133.0, 128.2, 119.8, 118.3, 112.4, 37.6, 35.5, 29.1, 22.2, 13.9; IR: 3470, 3064, 2958, 2867, 2231, 1610, 1506, 1462, 1414, 1381, 1115, 1021, 841 cm^{-1}; HRMS (ESI+): *m/z* $[M + H]^+$ calcd for $C_{13}H_{15}N_2$ 199.1230 ; found 199.1230.

*2-(pyridin-2-yl)hexanenitrile (**3i**).* Colorless oil; 86 mg (99%)*;* eluent mixture: pentane: diethyl ether (10:1 (v/v)); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.58 – 8.51 (m, 1H), 7.70 – 7.67 (m, 1H), 7.42 – 7.37 (m, 1H), 7.22 – 7.20 (m, 1H), 3.94 (dd, *J* = 8.3, 6.4 Hz, 1H), 1.99 – 1.95 (m, 2H), 1.53 – 1.25 (m, 4H), 0.86 (t, *J* = 7.4 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 155.4, 149.9, 137.3, 122.9, 121.7, 120.2, 39.9, 33.9, 29.1, 22.1, 13.8; IR: 3180, 2933, 2867, 2322, 1920, 1738, 1586, 1467, 1437, 1301, 1206, 994, 755, 665 cm^{-1}; HRMS (ESI+): *m/z* $[M]^+$ calcd for $C_{11}H_{14}N_2$, 174.1152; found 174.1145.

*2-(thiophen-2-yl)hexanenitrile (**3j**).* Yellowish oil*;* 58 mg (65%), ^{1}H NMR (600 MHz, CDCl3) δ 7.27 – 7.26 (m, 1H), 7.06 – 7.05 (d, *J* = 3.5 Hz, 1H), 6.98 – 6.97 (m, 1H), 4.06 (dd, *J* = 8.4, 6.3 Hz, 1H), 2.06 – 1.91 (m, 2H), 1.58 – 1.43 (m, 2H), 1.43 – 1.33 (m, 2H), 0.93 (t, *J* = 7.3 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 138.2, 127.1, 126.1, 125.5, 120.1, 35.7, 32.6, 29.1, 22.1, 13.9; IR: 3468, 3109, 2957, 2865, 2242, 1728, 1461, 1379, 1238, 1038, 836, 703 cm^{-1}; HRMS (ESI+): *m/z* $[M + Na]^+$ calcd for $C_{10}H_{13}N_1NaS$, 202.0661; found 202.0659.

*2,3-diphenylpropanenitrile (**4a**).*[10] Colorless oil; 89 mg (86%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41 – 7.26 (m, 8H), 7.18 – 7.14 (m, 2H), 4.02 (dd, *J* = 8.5, 6.4 Hz, 1H), 3.21 (dd, *J* = 13.6, 8.4 Hz, 1H), 3.15 (dd, *J* = 13.7, 6.4 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 136.4, 135.3, 129.3, 129.1, 128.7, 128.3, 127.6, 127.5, 120.5, 42.3, 39.9.

*3-phenyl-2-(pyridin-2-yl)propanenitrile (**4b**).*[13c] Yellowish oil; 76 mg (73%); eluent mixture: pentane: diethyl ether (10:1 (v/v)); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.65 – 8.64 (m, 1H), 7.68 – 7.65 (m, 1H), 7.30 – 7.24 (m, 5H), 7.18 – 7.16 (m, 2H), 4.21 (dd, *J* = 8.7, 5.9 Hz, 1H), 3.37 (dd, *J* = 13.6, 5.9 Hz, 1H), 3.26 (dd, *J* = 13.6, 8.7 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 154.6, 150.1, 137.3, 136.4, 129.3, 128.8, 127.5, 123.2, 122.3, 119.8, 42.2, 40.2.

*2-phenyl-3-(p-tolyl)propanenitrile (**4c**).*[14] White solid; 101 mg (91%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.33 (m, 3H), 7.29 – 7.28 (m, 2H), 7.13 – 7.11 (m, 2H), 7.06 – 7.04 (m, 2H), 3.99 (dd, *J* = 8.5, 6.3 Hz, 1H), 3.16 (dd, *J* = 13.7, 8.5 Hz, 1H), 3.11 (dd, *J* = 13.7, 6.4 Hz, 1H), 2.34 (s, 3H); $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 137.1, 135.4, 133.3, 129.4, 129.2, 129.1, 128.2, 127.6, 120.6, 41.9, 40.0, 21.2.

*3-(3,4-dimethoxyphenyl)-2-phenylpropanenitrile (**4d**).*[13c] Off-white solid; 121 mg (91%); eluent mixture: pentane: diethyl ether (10:1 (v/v)); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 – 7.30 (m, 3H), 7.26 – 7.22 (m, 2H), 6.78 – 6.79 (m, 1H), 6.71 – 6.69 (m, 1H), 6.52 – 6.51 (m, 1H), 3.98 (dd, *J* = 7.8, 6.4 Hz, 1H), 3.86 (s, 3H), 3.76 (s, 3H), 3.14 (dd, *J* = 13.7, 7.9 Hz, 1H), 3.09 (dd, *J* = 13.7, 6.4 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 148.8, 148.4, 135.3, 129.1, 128.7, 128.3, 127.7, 121.5, 120.6, 112.5, 111.2, 56.0, 55.9, 41.9, 40.0.

*3-(benzo[d][1,3]dioxol-4-yl)-2-phenylpropanenitrile (**4e**).* Colorless oil; 91 mg (72%); eluent mixture: pentane: diethyl ether (5:1 (v/v)); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.30 (m, 3H), 7.28 – 7.25 (m, 2H), 6.73 – 6.72 (m, 1H), 6.63 – 6.58 (m, 2H), 5.94 (s, 2H), 3.96 (dd, *J* = 8.4, 6.4 Hz, 1H), 3.10 (dd, *J* = 13.7, 8.3 Hz, 1H), 3.05 (dd, *J* = 13.8, 6.5 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 147.8, 147.0, 135.2, 130.0, 129.1, 128.3, 127.6, 122.6, 120.5, 109.6, 108.5, 101.2, 42.0, 40.1; IR: 3064, 3031, 2899, 2241, 1685, 1605, 1495, 1446, 1249, 1194, 1100, 1039, 810, 751, 699 cm^{-1}; HRMS (ESI+): *m/z* $[M + H]^+$ calcd for $C_{16}H_{14}O_2N$, 252.1019; found 252.1017.

*2-phenyl-3-(3-(trifluoromethyl)phenyl)propanenitrile (**4f**).* Colorless oil; 105 mg (76%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55 – 7.53 (m, 1H), 7.44 – 7.42 (m, 1H), 7.39 – 7.33 (m, 4H), 7.30 – 7.29 (m, 1H), 7.26 – 7.23 (m, 2H), 4.04 (dd, *J* = 8.1, 6.5 Hz, 1H), 3.25 (dd, *J* = 13.7, 8.1 Hz, 1H), 3.21 (dd, *J* = 13.7, 6.5 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 137.1, 134.6, 130.9 (q, *J* = 32.4 Hz), 129,3, 129,2, 128.6, 127.6, 126.2 (q, *J* = 3.8 Hz), 124.4 (q, *J* = 3.8 Hz), 123.9 (q, *J* = 272.2 Hz), 41.9, 39.5; ^{19}F NMR (282 MHz, $CDCl_3$) δ - 62.73; IR: 3066, 3035, 2933, 2243, 1599, 1495, 1451, 1330, 1166, 1126, 1075, 911, 792, 754, 701 cm^{-1}; HRMS (ESI+): *m/z* $[M + Na]^+$ calcd for $C_{16}H_{12}NF_3Na$, 298.0814; found 298.0814.

*3-(naphthalen-1-yl)-2-phenylpropanenitrile (**4g**).*[26b] Colorless oil; 107 mg (83%);^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 – 7.89 (m, 2H), 7.82 – 7.80 (m, 1H), 7.59 – 7.50 (m, 2H), 7.43 – 7.29 (m, 7H), 4.18 (dd, *J* = 8.7, 6.7 Hz, 1H), 3.70 – 3.57 (m, 2H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 135.8, 134.1, 132.4, 131.4, 129.4, 129.3, 128.5, 128.4, 128.3, 127.5, 126.7, 125.9, 125.6, 122.7, 120.6, 39.7, 39.0 ppm.

*2-phenyl-3-(pyridin-4-yl)propanenitrile (**4h**).*[14] Yellowish oil; 73 mg (70%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.62 – 8.60 (m, 1H), 7.65 – 7.62 (m, 1H), 7.37 – 7.36 (m, 4H), 7.34 – 7.30 (m, 1H), 7.23 – 7.20 (m, 1H), 7.15 – 7.14 (m, 1H), 4.50 (dd, *J* = 9.3, 6.6 Hz, 1H), 3.36 (dd, *J* = 13.9, 9.3 Hz, 1H), 3.30 (dd, *J* = 13.9, 6.6 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 156.1, 149.5, 136.9, 135.4, 129.1, 128.2, 127.4, 124.0, 120.5, 44.1, 37.3.

*2-phenyl-3-(pyridin-2-yl)propanenitrile (**4i**).*[10] Yellowish oil; 49 mg (47%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.61 – 8.59 (m, 1H), 7.62 – 7.60 (m, 1H), 7.36 – 7.35 (m, 4H), 7.34 – 7.29 (m, 1H), 7.21 – 7.18 (m, 1H), 7.13 – 7.12 (m, 1H), 4.48 (dd, *J* = 9.3, 6.5 Hz, 1H), 3.35 (dd, *J* = 13.9, 9.3 Hz, 1H), 3.28 (dd, *J* = 13.9, 6.5 Hz, 1H); $^{13}C\{^{1}H\}$ NMR

(151 MHz, $CDCl_3$) δ 156.3, 149.8, 136.9, 135.5, 129.2, 128.3, 127.5, 124.0, 122.5, 120.7, 44.3, 37.4.

*3-(furan-2-yl)-2-phenylpropanenitrile (**4j**).*[26c] Colorless oil; 62 mg (63%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.25 (m, 6H), 6.30 – 6.29 (m,1H), 6.12 – 6.11 (m, 1H), 4.15 (dd, *J* = 8.6, 6.5 Hz, 1H), 3.27 (dd, *J* = 15.0, 8.6 Hz, 1H), 3.19 – 3.13 (m, 1H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 150.1, 142.3, 135.0, 129.2, 128.7, 128.5, 110.6, 108.4, 37.2, 34.8.

*2-phenyl-3-(thiophen-2-yl)propanenitrile (**4k**).*[18] Colorless oil; 87 mg (82%),; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 – 7.26 (m, 5H), 7.17 (m, 1H), 6.92 (m, 1H), 6.85 (m, 1H), 4.04 (dd, *J* = 8.1, 6.4 Hz, 1H), 3.43 (dd, *J* = 14.8, 8.2 Hz, 1H), 3.34 (dd, *J* = 14.8, 6.3 Hz, 1H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 138.0, 134.8, 129.2, 128.5, 127.5, 127.2, 127.1, 125.0, 40.1, 36.2.

*2-phenylbutanenitrile (**4l**).*[12a] Colorless oil; 38 mg (52%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41 – 7.29 (m, 5H), 3.74 (t, *J* = 7.2 Hz, 1H), 1.97 – 1.92 (m, 2H), 1.08 (t, *J* = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 135.9, 129.1, 128.1, 127.4, 120.9, 39.0, 29.4, 11.6.

*2-phenyloctanenitrile (**4m**).*[10] Colorless oil; 94 mg (93%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.37 (m, 2H), 7.34 – 7.31 (m, 3H), 3.77 (dd, *J* = 8.7, 6.2 Hz, 1H), 1.97 – 1.82 (m, 2H), 1.55 – 1.42 (m, 2H), 1.36 – 1.25 (m, 6H), 0.88 (t, *J* = 6.9 Hz, 3H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 136.2, 129.1, 128.0, 127.3, 121.0, 37.5, 36.0, 31.6, 28.7, 27.0, 22.6, 14.1.

*4-methyl-2-phenylpentanenitrile (**4n**).*[13c] Colorless oil; 71 mg (82%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 – 7.30 (m, 5H), 3.81 (dd, *J* = 9.8, 6.4 Hz, 1H), 1.91 (ddd, *J* = 13.4, 9.8, 5.5 Hz, 1H), 1.88 – 1.80 (m, 1H), 1.64 (ddd, *J* = 13.3, 8.4, 6.3 Hz, 1H), 0.99 (dd, *J* = 8.0, 6.5 Hz, 6H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 136.4, 129.2, 128.1, 127.3, 121.1, 45.1, 35.61, 26.2, 22.7, 21.7.

*2-phenylhept-6-enenitrile (**4o**).*[26d] Colorless oil; 78 mg (78%); ^{1}H NMR (600 MHz, $CDCl_3$) δ δ 7.41 – 7.30 (m, 5H), 5.76 (ddt, *J* = 17.0, 10.2, 6.7 Hz, 1H), 5.05 – 4.97 (m, 2H), 3.79 (dd, *J* = 8.6, 6.2 Hz, 1H), 2.13 – 2.08 (m, 2H), 1.98 – 1.84 (m, 2H), 1.67 – 1.52 (m, 2H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 137.6, 136.0, 129.1, 128.1, 127.3, 120.9, 115.5, 37.3, 35.3, 33.0, 26.2.

*3-cyclohexyl-2-phenylpropanenitrile (**4p**).*[14]

Colorless oil; 77 mg (72%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 – 7.30 (m, 5H), 3.85 (dd, *J* = 10.1, 6.2 Hz, 1H), 1.92 – 1.81 (m, 2H), 1.78 – 1.62 (m, 5H), 1.57 – 1.49 (m, 1H), 1.31 – 1.13 (m, 3H), 1.01 - 0.92 (m, 2H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 136.6, 129.2, 128.0, 127.3, 121.2, 43.8, 35.4, 34.9, 33.4, 32.4, 26.4, 26.0, 25.9.

General procedure of *C*-methylation of nitriles

A glass Ace pressure tube (22 mL) equipped with a magnetic stir bar was charged with **Mn-2** (8 mg, 0.025 mmol), Cs_2CO_3 (16.3 mg, 0.05 mmol). A rubber septum was attached to the tube and the reaction vessel was evacuated and backfilled with argon for three times. Under an inert atmosphere nitrile (0.5 mmol), methanol (1 mL) and 1,4-dioxane (1 mL) were added and the tube was closed with a screw cap. The resulting mixture was stirred at 135 °C (aluminum block) for 24 h under argon atmosphere. Upon cooling down to room temperature the residue was directly purified by flash column chromatography on silica gel eluting with pentane:diethyl ether mixtures to give the pure desired product.

*2-phenylpropanenitrile (**5a**).*[26e] Yellowish oil; 46 mg (70%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41-7.31 (m, 5H), 3.90 (q, *J* = 7.3 Hz, 1H), 1.65 (d, *J* = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 137.2, 129.3, 128.2, 126.8, 121.7, 31.4, 21.6.

*2-(2-methoxyphenyl)propanenitrile (**5b**).*[26f]

Yellowish oil 52 mg (65%); eluent mixture: pentane: diethyl ether (10:1 (v/v)); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43-7.41 (m, 1H), 7.32-7.29 (m, 1H), 7.01-6.98 (m, 1H), 6.91-6.89 (m, 1H), 4.25 (q, *J* = 7.2 Hz, 1H), 3.87 (s, 3H), 1.58 (d, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 156.2, 129.4, 127.7, 125.5, 122.1, 121.1, 110.9, 55.6, 25.7, 19.6.

*2-(3-methoxyphenyl)propanenitrile (**5c**).*[26g] Yellowish oil 56 mg (70%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 (m, 1H), 6.94-6.93 (m, 1H), 6.89 (m, 1H), 6.87-6.85 (m, 1H), 3.87 (q, *J* = 7.3 Hz, 1H), 3.83 (s, 3H), 1.64 (d, *J* = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 160.2, 138.6, 130.3, 121.7, 119.1, 113.5, 112.7, 55.5, 31.4, 21.5.

*2-(4-methoxyphenyl)propanenitrile (**5d**).*[26e] Yellowish oil 48 mg (59%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30-7.28 (m, 2H), 6.94-6.91 (m, 2H), 3.87 (q, *J* = 7.4 Hz, 1H), 3.83 (s, 3H), 1.64 (d, *J* = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 159.4, 129.2, 128.0, 122.0, 114.6, 55.5, 30.6, 21.7.

*2-(2-chlorophenyl)propanenitrile (**5e**).*[26e] Yellowish oil; 51 mg (61%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58 (m, 1H), 7.41-7.39 (m, 1H), 7.36-7.32 (m, 1H), 7.30-7.27 (m, 1H), 4.36 (q, *J* = 7.1 Hz, 1H), 1.63 (d, *J* = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 134.9, 132.6, 130.2, 129.6 128.4, 127.9, 121.2, 29.0, 20.1.

*2-(4-chlorophenyl)propanenitrile (**5f**).*[26e] Yellowish oil; 57 mg (69%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38-7.35 (m, 2H), 7.31-7.28 (m, 2H), 3.88 (q, *J* = 7.4 Hz, 1H), 1.63 (d, *J* = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 135.6, 134.2, 129.5, 128.2, 121.3, 30.9, 21.5.

2-(pyridin-2-yl)propanenitrile (5g).[26h]

36 mg (55%), yellowish oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.62-8.61 (m, 1H), 7.77-7.74 (m, 1H), 7.48-7.47 (m, 1H), 7.29-7.27 (m, 1H), 4.08 (q, *J* = 7.4 Hz, 1H), 1.73 (d, *J* = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 156.2, 150.0, 137.6, 123.1, 121.2, 121.1, 33.9, 19.8.

*2-(thiophen-2-yl)propanenitrile (**5h**).*[26i] Yellowish oil; 42 mg (61%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28-7.27 (m, 1H), 7.08-7.07 (m, 1H), 6.99-6.98 (m, 1H), 4.18 (q, *J* = 7.4 Hz, 1H), 1.74 (d, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 139.3, 127.2, 125.7, 125.5, 120.8, 26.7, 21.6.

Representative procedure for gram-scale synthesis of 2-phenyl-3-(*p*-tolyl)propanenitrile (4c)

A glass pressure tube (25 mL) equipped with a magnetic stirrer was charged with **Mn-2** (35.2 mg, 0.055 mmol), Cs_2CO_3 (179.3 mg, 0.55 mmol). A rubber septum was attached to the tube and the reaction vessel was evacuated and backfilled with argon for three times. Under an inert atmosphere *p*-tolylmethanol (1.34 g, 11.0 mmol), 2-phenylacetonitrile (632 µL, 644 mg, 5.5 mmol) and toluene (5.5 mL) were added and the tube was closed with a screw cap. The resulting mixture was stirred at 135 °C (aluminum block) for 24 h under argon atmosphere. Upon cooling down to room temperature the residue was concentrated under reduced pressure and purified by flash column chromatography on silica gel eluting with pentane: diethyl ether (20:1 (v/v)) to give the pure **4c** (1022 mg, 84% yield).

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website: copies of NMR spectra (PDF)

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Notes

The authors declare no competing financial interests.

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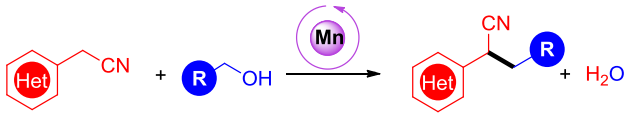

readily abandant feedstocks *value-added alkyl nitriles*

First row metal catalyst * Catalytic amount of base
**** Methanol as C1 source * High yield and excellent selectivity***