Direct Transformation of Primary Nitro Compounds into Nitriles with Sodium Dithionite

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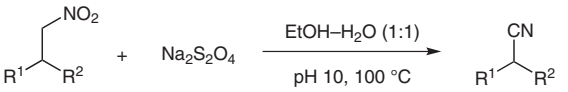
Abstract: A new and practical direct transformation of primary nitro compounds into nitriles with sodium dithionite is described. The reaction is simple, convenient and eliminates the use of expensive and moisture-sensitive reagents.

Key words: nitriles, sulfur, nitro compounds, synthetic methods, radicals

Nitriles are one of the most widely used building blocks in organic chemistry, and can be used to synthesize many functional groups such as carbonyl compounds, amines, and amides.[1] Synthetic methods employed for the preparation of alkyl nitriles include (i) reaction of alkyl halides with inorganic cyanides,[2] (ii) transition-metal-mediated cyanation,[3] (iii) conversion of aldehydes,[4] alcohols and amines,[5] (iv) dehydration of aldoximes and amides,[6] and (v) cyanation through C–H bond functionalization.[7] The direct transformation of primary nitro compounds into nitriles is an attractive alternative approach for the synthesis of alkyl nitriles. To date, many methods have been developed for the conversion of primary nitro compounds into nitriles by using different systems involving phosphorus compounds {P_2I_4,[8a] $(EtO)_2PCl$,[8b] and PCl_3[8c,d]}, sulfur compounds (SO_2[9a] and $Me_3SiSSiMe_3$[9b]), silyl derivatives such as Me_3SiI,[10] and radical chemistry.[11] Transformation of optically active nitroalkanes into chiral nitriles by using benzyl bromide, KOH and nBu$_4$NI was reported by Carreira et al.[12] However, although there are many methods available for this transformation, there is still a need for alternative synthetic approaches starting from easily accessible reagents and using mild reaction conditions.

Sodium dithionite is a readily available, inexpensive reducing agent that is capable of reducing a variety of functional groups, including diazonium salts, imines, oximes, aldehydes, ketones, and nitroso compounds.[13] The use of sodium dithionite in the reduction of aromatic nitro compounds to produce amines has also been known for a long time.[14] The reduction of tertiary nitro compounds to hydroxylamines, and aromatic nitro compounds into amines was reported by Park et al. with sodium dithionite in the presence of electron-transfer catalyst octylviologen.[14b] However, to the best of our knowledge, there is no report on the direct transformation of aliphatic nitro compounds into nitriles with sodium dithionite.

Herein, we report a very convenient method for the transformation of primary nitro compounds into nitriles by using sodium dithionite as reagent in a water–ethanol solvent system (Scheme 1). This method eliminates the need for moisture-sensitive, expensive, and highly toxic reagents such as metal cyanides. In addition, using inexpensive reagents with a water–ethanol solvent system instead of toxic organic solvents gives further advantages in terms of cost and environmental concerns.



Scheme 1 Transformation of primary nitro compounds into nitriles

In initial trials, we attempted to transform the nitro group of 2,2′-(2-nitroethane-1,1-diyl)bis(1*H*-pyrrole) (**1a**) into the corresponding nitrile by the reaction with sodium dithionite at different temperatures (Table 1, entries 1–4). Reactions of compound **1a** with four equivalents of sodium dithionite at room temperature and 50 °C in an ethanol–water mixture (1:1) did not give any product, even after 24 hours (Table 1, entries 1 and 2) and starting compound **1a** was recovered after the reactions. When the reaction was carried out at 80 °C, nitrile product **2a** was obtained as the sole product in low yield (20%; Table 1, entry 3). The yield was increased slightly to 25% by increasing the reaction temperature to 100 °C, and the increased temperature reduced the required reaction time so that the model reaction was completed in two hours (Table 1, entry 4). The reaction was monitored by TLC, and 2,2-di(1*H*-pyrrol-2-yl)acetonitrile (**2a**) was purified by flash column chromatography. Subsequently, the effect of solvents was investigated on the model reaction at 100 °C by using several high-boiling-point cosolvents such as dioxane, toluene, 1,2-dichloroethane (DCE), 2-propanol and *N*,*N*-dimethylformamide (DMF), however, these solvents gave the product in lower yields than those obtained by using the ethanol–water solvent system (Table 1, entries 5–9).

The reaction was then performed with different amounts of sodium dithionite in ethanol–water at 100 °C (Table 2). The yield of the product **2a** was increased when the amount of $Na_2S_2O_4$ was increased to 20 equivalents (Table 2, entries 1–4); it was determined that this amount of

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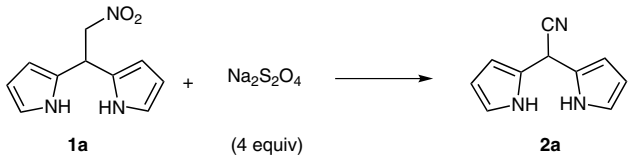
Table 1 Optimization of Reaction Temperature and Solvent[a]

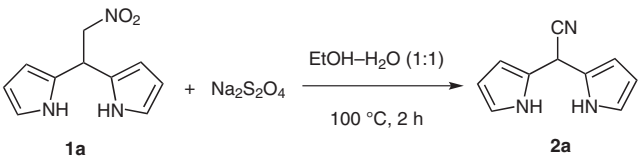


1a **2a**

Entry	Temp (°C)	Solvent (1:1)	Time (h)	Yield (%)[b]
1	r.t.	EtOH–H_2O	24	–
2	50	EtOH–H_2O	24	–
3	80	EtOH–H_2O	10	20
4	100	EtOH–H_2O	2	25
5	100	dioxane–H_2O	2	18
6	100	toluene–H_2O	2	10
7	100	DCE–H_2O	2	15
8	100	*i*-PrOH–H_2O	2	20
9	100	DMF–H_2O	2	15

[a] All reactions were performed by using 1 mmol of substrate **1a**.
[b] Isolated yield after flash chromatography.

Table 2 Optimization of the Reaction Conditions[a]



1a **2a**

Entry	$Na_2S_2O_4$ (equiv)	pH	Yield (%)[b]
1	4	7	25
2	10	7	27
3	20	7	30
4	30	7	30
5	20	8	30
6	20	9	35
7	20	10	48
8	20	11	40
9	20	12	41

[a] All reactions were performed by using 1 mmol of substrate **1a**.
[b] Isolated yield after flash chromatography.

sodium dithionite was sufficient to complete the reaction when added in portions to minimize decomposition in aqueous solution. It is known that the pH of the reaction medium is an important parameter for sodium dithionite mediated reduction reactions. The reduction of aldehydes and ketones by sodium dithionite is reported at high pH values, obtained by using $NaHCO_3$ or buffer solutions, to prevent rapid decomposition of $Na_2S_2O_4$, which is sensitive to acid.[15] The critical role of pH on sodium dithionite prompted us to examine the model reaction at higher pH values (Table 2, entries 5–9) and the highest yield was obtained at pH 10 (48% yield; Table 2, entry 7).

To illustrate the applicability of this reaction, a range of aryl and alkyl substituted primary nitro compounds **1a**–**p** were treated with sodium dithionite under the optimized reaction conditions [20 equiv $Na_2S_2O_4$, pH 10, EtOH–H_2O (1:1), 100 °C]; the results are presented in Table 3. We found that the reaction is general with respect to aryl substituents such as pyrrolyl, thionyl, furyl, phenyl and indolyl (Table 3, entries 1–7). All substrates with aryl groups furnished the corresponding products in comparable yields (45–60%). The electron-donating or electron-withdrawing nature of substituents on the phenyl group did not change the yields of the reaction significantly. As shown in Table 3 (entries 8–13), the substituents on the aromatic ring had little impact on the yields of the desired nitrile products, which were obtained in 48–55% yield. When mono aryl substituted (Table 3, entry 14) and alkyl substituted nitro compounds were used (Table 3, entries 15 and 16), a small decrease in reaction yield was observed and the corresponding products were isolated in 32–42% yield. All reactions performed at 100 °C furnished nitrile compounds as the main products. All starting materials were consumed in the reactions and no products other than the expected nitrile compounds could be identified. The structures of new products were determined by ^1H, ^{13}C NMR, FTIR and HRMS analysis.

Table 3 Transformation of Primary Nitro Compounds into Nitriles[a]

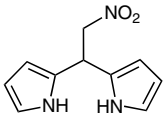
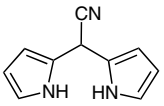
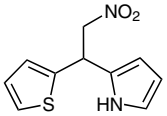
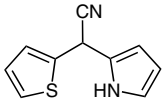
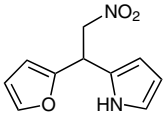
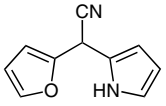
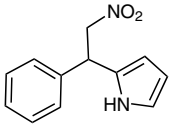
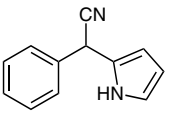
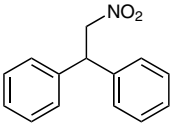
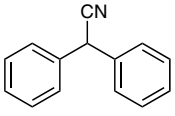
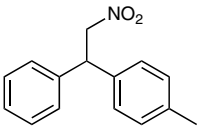
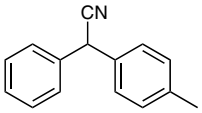
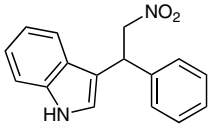
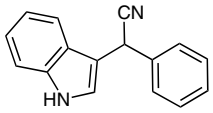
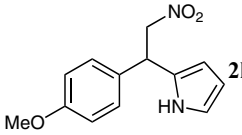
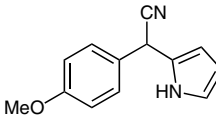
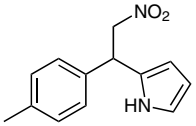
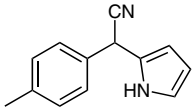
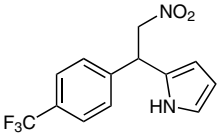
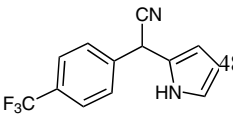
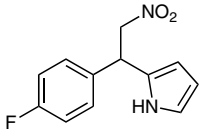
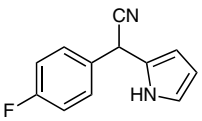
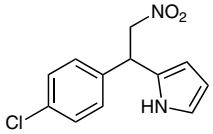
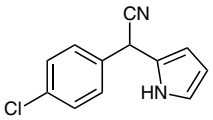
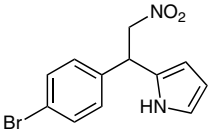
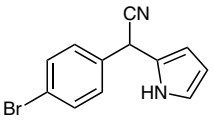
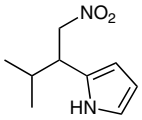
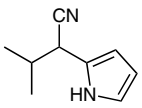
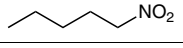
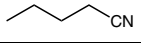
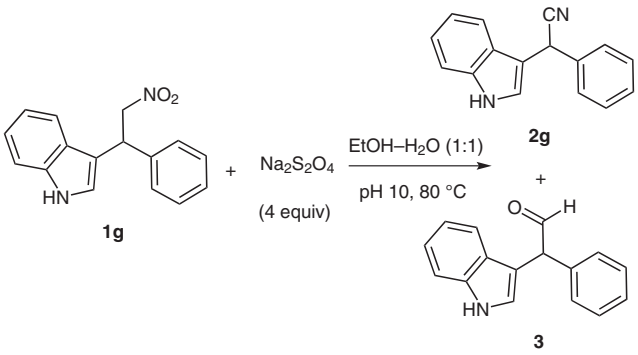
Entry	Substrate	Product	Yield (%)[b]
1	**1a** 	**2a** 	48
2	**1b** 	**2b** 	54
3	**1c** 	**2c** 	47
4	**1d** 	**2d** 	55
5	**1e** 	**2e** 	52

Table 3 Transformation of Primary Nitro Compounds into Nitriles[a] (continued)

Entry	Substrate	Product	Yield (%)[b]
6	**1f** 	**2f** 	45
7	**1g** 	**2g** 	60
8	**1h** 	**2h** 	50
9	**1i** 	**2i** 	55
10	**1j** 	**2j** 	48
11	**1k** 	**2k** 	48
12	**1l** 	**2l** 	50
13	**1m** 	**2m** 	55
14	**1n** 	**2n** 	42
15	**1o** 	**2o**	40
16	**1p** 	**2p** 	32

[a] All reactions were performed by using 1 mmol of substrate **1** at pH 10.
[b] Isolated yield after flash chromatography.

We then turned our attention to the mechanism of this interesting transformation. In this context, we repeated the reaction of 3-(2-nitro-1-phenylethyl)-1*H*-indole (**1g**) with only four equivalents of sodium dithionite at lower temperature (80 °C). The reaction was monitored by TLC and stopped before all starting material had reacted. The reaction proceeded smoothly and produced the corresponding product **2g** in 30% yield with a minor amount of 2-(1*H*-indol-3-yl)-2-phenylacetaldehyde (**3**) produced in 12% yield (Scheme 2). Previously, Pojer reported the reaction of oximes with aqueous sodium dithionite at room temperature that gave a similar type of carbonyl compound.[16]

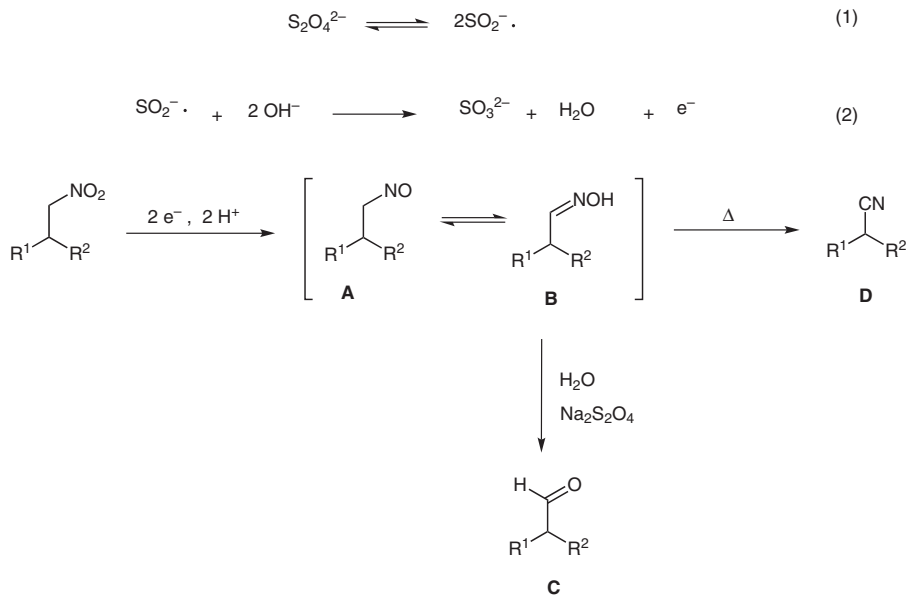


Scheme 2 Transformation reaction at 80 °C

Although details of the mechanism remain unclear, based on the above experimental results, together with reports on the mechanism of other sodium dithionite reactions,[15] a plausible mechanism for the transformation of the nitro group into a nitrile is tentatively proposed in Scheme 3. The mechanism of dithionite decomposition and the distribution of its thermal decomposition products have been documented extensively. The thermal decomposition of $Na_2S_2O_4$ gives the ESR-detectable sulfur dioxide radical anion ($SO_2^{\bullet-}$), which is in equilibrium with dithionite anion [Scheme 3, eq. 1].[17] The radical anion affords the sulfite anion (SO_3^{2-}) and acts as an electron donor in alkaline solutions [Scheme 3, eq. 2].[18] Nitroso alkyl is a possible reduction product of nitro compounds.[14b] In light of the foregoing precedent, the first step can be assumed to be the electron-transfer-reduction of diaryl substituted nitro to give the nitroso compound **A**, which forms more stable tautomeric oxime intermediate **B**.[19] Reaction of the latter intermediate **B** in the reaction medium affords aldehyde **C** and, especially at high temperature, nitrile compound **D**.[20]

In summary, we have performed the first direct transformation of primary nitro compounds into nitriles by the application of sodium dithionite. This transformation allowed the synthesis of a range of novel nitrile compounds. The method operates under mild reaction conditions, in a water-containing solvent system with an inexpensive, readily available reagent, and is superior to the existing methodologies because it does not require a transition-metal catalyst or anhydrous reaction medium.

^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded in $CDCl_3$ with a Bruker Ultrashield FT NMR spectrometer. Data for ^{1}H NMR are reported as follows: chemical shift (δ, ppm) and multiplicity (s = singlet, d = doublet, t = triplet, dd = doublet of doublet, m = multiplet, br s = broad singlet). Coupling constants are expressed as *J* values in hertz. Infrared spectra were recorded with an ATR (Nicolet iS10) instrument and are reported in cm^{-1}; only



Scheme 3 Proposed mechanism for the transformation

representative absorptions are given. Mass spectra were recorded with an Agilent Technologies 6224 TOF LC/MS. Flash column chromatography was performed on silica gel 60 (230–400 mesh). Reactions were monitored by thin-layer chromatography using 60 F_{254} silica gel plates. Visualization was accomplished with UV light, phosphomolybdic acid and/or anisaldehyde. Commercially available reagents and solvents were used without further purification. Buffer solutions were prepared as follows: potassium dihydrogen orthophosphate/sodium hydroxide for pH 7, sodium tetraborate/hydrochloric acid buffer for pH 8, sodium tetraborate/sodium hydroxide for pH 9 and 10, sodium hydrogen orthophosphate/sodium hydroxide for pH 11. Primary nitro compounds **1a**–**n** were synthesized according to reported procedures.[21]

Synthesis of Nitrile Compounds; General Procedure

To a stirred solution of sodium dithionite (0.7 g, 4 mmol) in buffer solution (3 mL, pH 10) was added a solution of nitro compound (1 mmol) in EtOH (3 mL) at r.t. and the mixture was heated to 100 °C. Excess sodium dithionite (2.8 g, 16 mmol) was added in portions during 2 h at this temperature, then the resulting mixture was cooled to r.t. and EtOAc (10 mL) was added. The aqueous layer was extracted with EtOAc (3 × 10 mL) and the organic phase was dried over $MgSO_4$. The solvent was then removed under reduced pressure and the crude product was purified by flash column chromatography on silica gel (EtOAc–hexane).

2,2-Di(1*H*-pyrrol-2-yl)acetonitrile (2a)

Yield: 82 mg (48%); brown viscous oil; R_f = 0.31 (EtOAc–hexane, 1:3).

IR (ATR): 2243 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 5.24 (s, 1 H, CHCN), 6.14 (br s, 2 H, C3-H), 6.20 (br s, 2 H, C4-H), 6.67 (br s, 2 H, C5-H), 8.04 (br s, 2 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.1, 108.5, 109.3, 117.6, 119.4, 122.9.

HRMS (APCI): *m/z* $[M - H]^-$ calcd for $C_{10}H_8N_3$: 170.0724; found: 170.0723.

2-(1*H*-Pyrrol-2-yl)-2-(thiophen-2-yl)acetonitrile (2b)

Yield: 102 mg (54%); orange viscous oil; R_f = 0.39 (EtOAc–hexane, 1:3).

IR (ATR): 2203 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 5.45 (s, 1 H, CHCN), 6.15 (dd, *J* = 2.9, 5.9 Hz, 1 H, pyrrole C3-H), 6.22 (br s, 1 H, pyrrole C4-H), 6.67 (br s, 1 H, pyrrole C5-H), 6.91–6.98 (m, 1 H, thiophene C3-H), 7.10–7.11 (m, 1 H, thiophene C4-H), 7.28 (d, *J* = 5.1 Hz, 1 H, thiophene C5-H), 8.18 (br s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.7, 108.7, 109.4, 117.6, 119.3, 123.74, 126.6, 126.8, 127.2, 137.3.

HRMS (APCI): *m/z* $[M - H]^-$ calcd for $C_{10}H_7N_2S$: 187.0335; found: 187.0339.

2-(Furan-2-yl)-2-(1*H*-pyrrol-2-yl)acetonitrile (2c)

Yield: 81 mg (47%); brown viscous oil; R_f = 0.45 (EtOAc–hexane, 1:3).

IR (ATR): 2211 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 5.25 (s, 1 H), 6.10–6.13 (m, 1 H), 6.18 (br s, 1 H), 6.27–6.31 (m, 2 H), 6.72 (br s, 1 H), 7.35 (s, 1 H), 8.26 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.5, 107.3, 107.5, 108.1, 109.8, 116.5, 118.3, 128.9, 142.5, 153.2.

HRMS (APCI): *m/z* $[M - H]^-$ calcd for $C_{10}H_7N_2O$: 171.0564; found: 171.0564.

2-Phenyl-2-(1*H*-pyrrol-2-yl)acetonitrile (2d)

Yield: 100 mg (55%); colorless viscous oil; R_f = 0.50 (EtOAc–hexane, 1:3).

IR (ATR): 2230 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 5.18 (s, 1 H, CHCN), 6.11 (br s, 2 H, pyrrole C3-H, C4-H), 6.68 (br s, 1 H, pyrrole C5-H), 7.32–7.37 (m, 5 H, Ph-H), 8.12 (br s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 36.3, 108.7, 109.3, 118.5, 119.2, 124.3, 127.7, 128.6, 129.3, 134.5.

HRMS (APCI): *m/z* $[M - H]^-$ calcd for $C_{12}H_9N_2$: 181.0771; found: 181.0776.

2,2-Diphenylacetonitrile (2e)[22]

Yield: 100 mg (52%); yellow solid; mp 73–74 °C (Lit.[22] 72–73 °C).

^1H NMR (400 MHz, $CDCl_3$): δ = 5.14 (s, 1 H, CHCN), 7.30–7.40 (m, 10 H, Ph-H).

HRMS (APCI): *m*/*z* [M – H]$^-$ calcd for $C_{14}H_{10}N$: 192.0819; found: 192.0822.

2-Phenyl-2-*p*-tolylacetonitrile (2f)[22]
Yield: 93 mg (45%); yellow solid; mp 60–61 °C (Lit.[22] 61–62 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.22 (s, 3 H, CH_3), 4.80 (s, 1 H, CHCN), 7.10–7.30 (m, 9 H, Ph-H).

HRMS (APCI): *m*/*z* [M – H]$^-$ calcd for $C_{15}H_{12}N$: 206.0975; found: 206.0978.

2-(1*H*-indol-3-yl)-2-phenylacetonitrile (2g)
Yield: 139 mg (60%); colorless viscous oil; R_f = 0.50 (EtOAc–hexane, 1:10).

IR (ATR): 2243 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.32 (s, 1 H, CHCN), 7.03–7.08 (m, 2 H, Ar-H), 7.16–7.19 (m, 1 H, Ar-H), 7.28–7.36 (m, 4 H, Ar-H), 7.39–7.41 (m, 3 H, Ar-H), 8.19 (br s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 34.5, 110.9, 111.6, 118.8, 119.7, 120.3, 122.9, 123.2, 125.3, 127.7, 128.1, 129.0, 135.5, 136.6.

HRMS (APCI): *m*/*z* [M – H]$^-$ calcd for $C_{16}H_{11}N_2$: 231.0928; found: 231.0926.

2-(4-Methoxyphenyl)-2-(1*H*-pyrrol-2-yl)acetonitrile (2h)
Yield: 106 mg (50%); yellow viscous oil; R_f = 0.42 (EtOAc–hexane, 1:3).

IR (ATR): 2235 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.80 (s, 3 H, OCH_3), 5.14 (s, 1 H, CHCN), 6.12 (br s, 2 H, pyrrole C3-H, C4-H), 6.70 (br s, 1 H, pyrrole C5-H), 6.90 (d, *J* = 8.6 Hz, 2 H, Ph-H), 7.25 (d, *J* = 8.6 Hz, 2 H, Ph-H), 7.97 (br s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 35.6, 55.3, 108.5, 109.4, 114.7, 118.6, 119.0, 124.8, 126.3, 128.9, 159.8.

HRMS (APCI): *m*/*z* [M – H]$^-$ calcd for $C_{13}H_{11}N_2O$: 211.0877; found: 211.0882.

2-(1*H*-Pyrrol-2-yl)-2-*p*-tolylacetonitrile (2i)
Yield: 108 mg (55%); brown viscous oil; R_f = 0.55 (EtOAc–hexane, 1:3).

IR (ATR): 2247 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.36 (s, 3 H, CH_3), 5.15 (s, 1 H, CHCN), 6.11 (br s, 2 H, pyrrole C3-H, C4-H), 6.68 (br s, 1 H, pyrrole C5-H), 7.17 (d, *J* = 8.1 Hz, 2 H, Ph-H), 7.23 (d, *J* = 8.1 Hz, 2 H, Ph-H), 8.00 (br s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2, 36.0, 108.5, 109.3, 118.6, 119.0, 124.6, 127.6, 130.0, 131.5, 138.4.

HRMS (APCI): *m*/*z* [M – H]$^-$ calcd for $C_{13}H_{11}N_2$: 195.0928; found: 195.0936.

2-(1*H*-Pyrrol-2-yl)-2-[4-(trifluoromethyl)phenyl]acetonitrile (2j)
Yield: 120 mg (48%); brown viscous oil; R_f = 0.58 (EtOAc–hexane, 1:3).

IR (ATR): 2243 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.27 (s, 1 H, CHCN), 6.11 (br s, 1 H, pyrrole C3-H), 6.14–6.16 (m, 1 H, pyrrole C4-H), 6.75 (br s, 1 H, pyrrole C5-H), 7.49 (d, *J* = 8.2 Hz, 2 H, Ph-H), 7.66 (d, *J* = 8.2 Hz, 2 H, Ph-H), 8.09 (br s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 36.2, 109.3, 109.7, 117.8, 119.7, 119.7 (q, $^1J_{C–F}$ = 271.0 Hz), 126.4 (q, $^3J_{C–F}$ = 3.7 Hz), 128.1, 128.8, 131.3 (q, $^2J_{C–F}$ = 33.0 Hz), 138.5.

HRMS (APCI): *m*/*z* [M – H]$^-$ calcd for $C_{13}H_8F_3N_2$: 249.0645; found: 249.0657.

2-(4-Fluorophenyl)-2-(1*H*-pyrrol-2-yl)acetonitrile (2k)
Yield: 96 mg (48%); colorless viscous oil; R_f = 0.48 (EtOAc–hexane, 1:3).

IR (ATR): 2239 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.15 (s, 1 H, CHCN), 6.05 (br s, 1 H, pyrrole C3-H), 6.09–6.11 (m, 1 H, pyrrole C4-H), 6.68 (br s, 1 H, pyrrole C5-H), 7.00–7.04 (m, 2 H, Ph-H), 7.26–7.29 (m, 2 H, Ph-H), 8.32 (br s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 35.4, 108.7, 109.1, 116.2 (d, $^2J_{C–F}$ = 22.0 Hz), 118.6, 119.4, 124.0, 129.5 (d, $^3J_{C–F}$ = 8.0 Hz), 130.2 (d, $^4J_{C–F}$ = 3.0 Hz), 162.6 (d, $^1J_{C–F}$ = 247.0 Hz).

HRMS (APCI): *m*/*z* [M – H]$^-$ calcd for $C_{12}H_8FN_2$: 199.0677; found: 199.0674.

2-(4-Chlorophenyl)-2-(1*H*-pyrrol-2-yl)acetonitrile (2l)
Yield: 108 mg (50%); brown viscous oil; R_f = 0.45 (EtOAc–hexane, 1:3).

IR (ATR): 2251 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.18 (s, 1 H, CHCN), 6.13 (br s, 1 H, pyrrole C3-H), 6.15–6.17 (m, 1 H, pyrrole C4-H), 6.73 (br s, 1 H, pyrrole C5-H), 7.26 (d, *J* = 8.4 Hz, 2 H, Ph-H), 7.34 (d, *J* = 8.4 Hz, 2 H, Ph-H), 8.17 (br s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 35.5, 108.7, 109.0, 118.4, 119.5, 123.7, 128.9, 129.4, 132.7, 134.6.

HRMS (APCI): *m*/*z* [M – H]$^-$ calcd for $C_{12}H_8ClN_2$: 215.0381; found: 215.0392.

2-(4-Bromophenyl)-2-(1*H*-pyrrol-2-yl)acetonitrile (2m)
Yield: 144 mg (55%); brown viscous oil; R_f = 0.45 (EtOAc–hexane, 1:3).

IR (ATR): 2242 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.13 (s, 1 H, CHCN), 6.06 (br s, 1 H, pyrrole C3-H), 6.11 (br s, 1 H, pyrrole C4-H), 6.69 (br s, 1 H, pyrrole C5-H), 7.18 (d, *J* = 8.3 Hz, 2 H, Ph-H), 7.47 (d, *J* = 8.3 Hz, 2 H, Ph-H), 8.29 (br s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 35.7, 108.8, 109.2, 118.2, 119.5, 122.8, 123.6, 129.2, 132.4, 133.5.

HRMS (APCI): *m*/*z* [M – H]$^-$ calcd for $C_{12}H_8BrN_2$: 258.9876; found: 258.9881.

3-Methyl-2-(1*H*-pyrrol-2-yl)butanenitrile (2n)
Yield: 62 mg (42%); yellow viscous oil; R_f = 0.45 (EtOAc–hexane, 1:6).

IR (ATR): 2235 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.99 (d, *J* = 4.9 Hz, 3 H, CH_3), 1.01 (d, *J* = 4.9 Hz, 3 H, CH_3), 2.03–2.11 [m, 1 H, $CH(CH_3)_2$], 3.72 (d, *J* = 5.9 Hz, 1 H, CHCN), 6.04 (br s, 1 H, pyrrole C3-H), 6.09–6.13 (m, 1 H, pyrrole C4-H), 6.69 (br s, 1 H, pyrrole C5-H), 8.14 (br s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.1, 20.4, 33.0, 38.6, 107.8, 109.1, 118.1, 119.0, 123.9.

HRMS (APCI): *m*/*z* [M – H]$^-$ calcd for $C_9H_{11}N_2$: 147.0928; found: 147.0931.

Acetonitrile (2o)
Yield: 16 mg (40%); colorless liquid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.00 (s, 3 H, CH_3).

Pentanenitrile (2p)[23]
Yield: 27 mg (32%); colorless liquid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.02 (t, *J* = 5.9 Hz, 3 H, CH_3), 1.47–1.54 (m, 2 H, CH_2CH_3), 1.64–1.74 (m, 2 H, $CH_2CH_2CH_2$), 2.30 (t, *J* = 5.9 Hz, 2 H, CH_2CN).

HRMS (APCI): *m*/*z* [M – H]$^-$ calcd for C_5H_8N: 82.0662; found 82.0663.

2-(1*H*-Indol-3-yl)-2-phenylacetaldehyde (3)
Yield: 28 mg (12%); colorless viscous oil; R_f = 0.55 (EtOAc–hexane 1:10).

IR (ATR): 1712 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.08 (s, 1 H, CHCO), 7.02–7.35 (m, 10 H, Ar-H), 8.13 (br s, 1 H, NH), 9.90 (s, 1 H, CHO).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 56.1, 110.9, 111.1, 119.1, 119.9, 122.5, 122.9, 126.6, 127.4, 128.7, 128.9, 136.0, 136.2, 197.1.

HRMS (APCI): *m*/*z* [M – H]$^-$ calcd for $C_{16}H_{12}NO$: 234.0924; found: 234.0927.

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