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One-Pot Synthesis of α-Amino Nitrile Units through Alkylative Strecker Cyanation from Formamides

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In this work, we describe the one-pot synthesis of α-amino nitrile units by the concomitant addition of alkyl (or aryl) Grignard reagents and TMS cyanide through alkylative Strecker cyanation from readily available formamides. The reaction is broad in scope and the conditions are mild, inexpensive, and easy to set-up, providing numerous α-amino nitriles in good yields (34 examples, 41–94% yield).

Introduction

α-Amino nitrile bi-functionality is an original moiety which can be encountered in a wide array of pharmaceuticals or natural compounds exhibiting biological activities.[1] This scaffold is a convenient precursor for the synthesis of unnatural amino-acids.

In addition, since they possess both nitrile and amino groups on the same carbon atom, α-amino nitrile units are also regarded as attractive and versatile synthetic tools, and for this reason, access to such moieties has been intensively studied.

The most common way employed for their synthesis is the racemic or enantioselective Strecker reaction.[2] Remarkable complementary methodologies such as C–H cyanation of amines have recently emerged.[3] Likewise, another original and smart way, relies on a reductive Strecker-type reaction (reductive cyanation) of amide or lactam. This approach is particularly relevant since amide functionality is ubiquitous and can be found in agrochemicals, natural products or pharmaceutical agents. Thus, one synthetic way able to chemoselectively transform this function would constitute a powerful tool for late-stage functionalization. In this field, we can mention the elegant works reported by Dixon group using Vaska's catalyst[4] as well as by Adolfsson group with $Mo(CO)_6$ catalyst (Scheme 1).[5] The common point of both methodologies relies on the formation of hemiaminal species by hydrosilylation reaction onto the amide and subsequent elimination leading to a reactive iminium intermediate which can be trapped by a nucleophile like cyanide.

The conversion of amide into iminium intermediate has also been described by using titanium hydride obtained from inexpensive $Ti(OiPr)_4$ and a silane reagent.[6] Inspired by this result, Tokuyama *et al.* used a combination of $Ti(OiPr)_4$ and Ph_2SiH_2 for the one-pot reductive allylation of amides in the course of the total synthesis of (−)-castoramine.[7] A similar approach was described by De Meijere and coworkers through their work on alkylation of dialkylformamides for the synthesis of tertiary *sec*-alkylamines.[8] However, geminal disubstitution of formamide[9] from a sequence of alkylation, formation of an iminium species and subsequent attack by a cyanide anion in a one-pot process has, to the best of our knowledge, never been reported for the synthesis of α-amino nitriles (Scheme 1).[10] Therefore, despite the numerous existing methods leading to α-amino nitrile units, discovery of new inexpensive and easy to set-up methodologies remains of primary interest. To this purpose, we propose herein a complementary access to α-amino nitrile function through an unprecedented one-pot reductive-Strecker reaction on formamides. We postulated that the combination of Grignard reagent, TMSCN and $Ti(OiPr)_4$ could promote the synthesis of α-amino nitriles in one-pot fashion from simple and readily available formamide[11] (Scheme 1).

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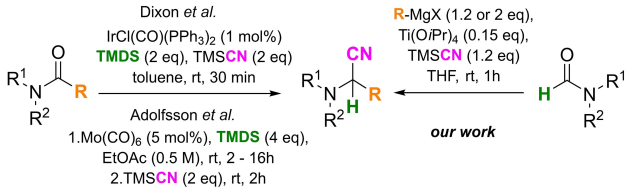


Scheme 1. Access to α-amino nitrile function by reductive Strecker type reaction.

Results and Discussion

We started a short optimization study on DMF as model substrate, using 4-methoxyphenyl magnesium bromide (1.0 M in THF), TMSCN and Ti(O*i*Pr)$_4$.

At the very beginning, Ti(O*i*Pr)$_4$ (0.05 eq) was used, ^{1}H-NMR conversion of compound **1** and **2** were 68% and 20%, respectively (entry 1). To our delight, employing TMSCN (1.2 eq), 4-methoxyphenyl magnesium bromide (1.2 eq) and Ti(O*i*Pr)$_4$ (0.15 eq) at room temperature yielded 2-(dimethylamino)-2-(4-methoxyphenyl)acetonitrile **1** with a very good conversion (88%, entry 2). However, when the amount of Ti(O*i*Pr)$_4$ was increased to 0.5 eq, the yield decreased and a messy crude was observed (entry 3). Without Ti(O*i*Pr)$_4$ (entry 4), a modest conversion (54%) into **1** was obtained along with a non-negligible amount of elimination product resulting in the formation of *p*-anisaldehyde **2** (34%). Increasing the amount of TMSCN (entry 5) or Grignard reagent (entry 6) to 2 equivalents led to similar conversions (respectively 83% and 86%). Next, we examined the influence of different solvents. Running the reaction in toluene resulted in a slight decrease of the conversion (72%, entry 7) while employing 1,4-dioxane or MTBE dramatically diminished the conversion (respectively 58% and 21%, entry 8 and 9) with concomitant formation of *p*-anisaldehyde (10% and 20%). Finally, result with MeTHF was similar to that observed with THF (88%, entry 10). With the optimized conditions in hand, we studied the scope of the reaction on different formamides (Figure 1).

The addition of aromatic Grignard reagents under conditions A (1.2 eq. R-MgX, 1.2 eq. TMSCN and 0.15 eq.Ti(O*i*Pr)$_4$) led to the corresponding α-amino nitriles in good yields (**3**, 88% and **4**, 92%). However, when the same conditions were used with benzyl-, cyclopropyl- or cyclohexylmagnesium chloride, the reaction turned out to be sluggish and incomplete conversions were observed. To overcome this issue, enhance of the amount of Grignard reagent was envisioned. By applying conditions B (2.0 eq. R-MgX., 1.2 eq. TMSCN and 0.15 eq. Ti(O*i*Pr)$_4$), the expected compounds **5** (84%), **6** (73%) and **7** (90%) were obtained in satisfactory yields. Similar difficulties were also encountered under conditions A for other examples and we decided to manage all the reactions under conditions B for the scope study.

Compared to DMF, products were obtained in similar yields when reactions were performed on diethylformamide with aromatic (**8**, 91%, **9**, 72% and **10**, 65%) or benzylic Grignard reagents (**11**, 48%). Reactions carried out on formamide with longer chains like *N,N-n*-dibutylformamide also delivered expected compounds in good yields (**12**, 72% and **13**, 70%). To our delight, conditions B were also suitable for bulkier formamides such as *N,N*-di-isopropylformamide and satisfying yields were obtained with aromatic Grignard reagents (**14**, 94% and **15**, 61%). We can notice that the vast majority of reactions is clean and, as an example, diamine **15** could be obtained after reduction performed on a crude mixture since the α-aminonitrile intermediate was found unstable.[12] Cyclic formamide like N-formylpiperidine showed good reactivity and addition of aromatic, benzylic or aliphatic Grignard reagents allowed the

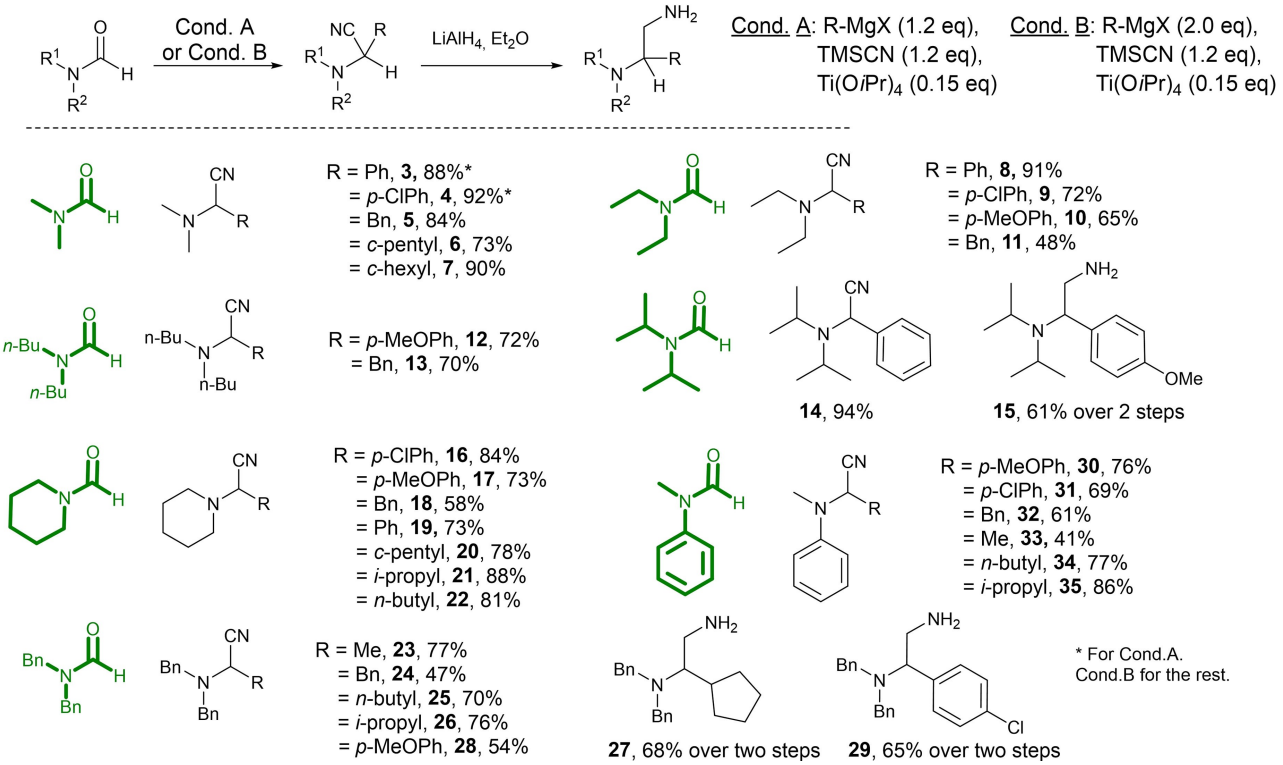


Figure 1. Scope of the reaction.

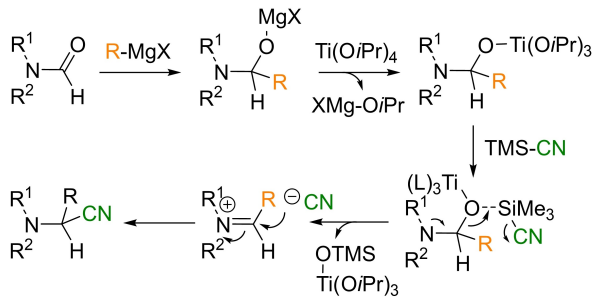
formation of the corresponding α-amino nitriles in good yields (respectively **16**, 84%, **17**, 73%, **18**, 58%, **19**, 73%, **20**, 78%, **21**, 88% and **22**, 81%). A similar behavior was also observed with *N,N*-dibenzylformamide since the addition of an array of organomagnesium compounds such as methyl, benzyl-, *n*-butyl-, isopropyl- or cyclopentylmagnesium halides delivered the expected compounds in good yields (**23**, 77%, **24**, 47%, **25**, 70%, **26**, 76% and **27**, 68%). Similarly, *p*-methoxyphenyl- and *p*-chlorophenylmagnesium bromides afforded the desired compounds **28**, 54% and **29**, 65%. Finally, we examined *N*-methylformanilide, a more challenging substrate, due to its propensity to undergo addition/elimination during the addition of the organometallic reagent. We were pleased to observe good yields by applying conditions B with aliphatic or aromatic Grignard reagents (**30**, 76%, **31**, 69%, **32**, 61%, **33**, 41%, **34**, 77% and **35**, 86%). The results obtained herein appeared particularly interesting since formamide has previously been used as formylating agent in the presence of Grignard reagents.[13]

Regarding the synthetic pathway, we proposed the following mechanism (Scheme 2). At first, addition of the organomagnesium halide onto the carbonyl moiety followed by a transmetallation by titanium isopropoxide would occur. At this stage, TMSCN could activate the carbon-oxygen bond allowing the formation of the iminium species with the concomitant release of the cyanide ion. Then the cyanide would react with the iminium intermediate affording the expected α-amino nitrile. The precise role of the titanium in this reaction is not fully determined. Indeed, it can act as a Lewis acid in order to activate the carbonyl group. But according to the optimization conditions (see Table 1), it seems to prevent the undesired elimination process leading to the derived amine probably by acting as a stabilizing agent.[14] In addition, when organomagnesium compounds possessing H in β position were used, a Ti(II) species could be generated, as used in the Kulinkovich reaction.[15]

The straightforward synthesis of α-amino nitriles could also constitute an interesting way for further functionalizations. Thus, from compound **1**, we can perform a methylation reaction (Scheme 3, way a) delivering a quaternary center in α position to the amine (compound **37**).

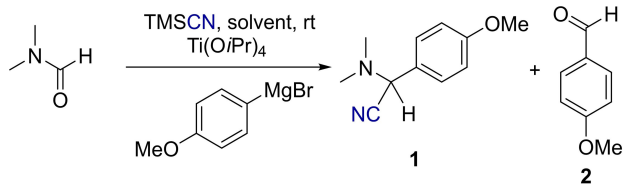
Nitrile could be also employed as a leaving group and be displaced by phenylmagnesium bromide (Scheme 3, way b, compound **36**). In addition modification of the nitrile moiety can be considered such as reduction by $LiAlH_4$ to provide the corresponding amine **39** (Scheme 3, way c), or the use of oxidative conditions, to reach an amide function (Scheme 3, way d compound **38**).

We tried to extend the scope of this reaction to secondary formamides or amides but unfortunately, so far, our conditions have revealed ineffective. The lack of reactivity towards amides could be explained by disadvantageous steric and/or electronic effects whereas concerning secondary formamides we postulated a deleterious deprotonation on the nitrogen thus prohibiting the reaction.



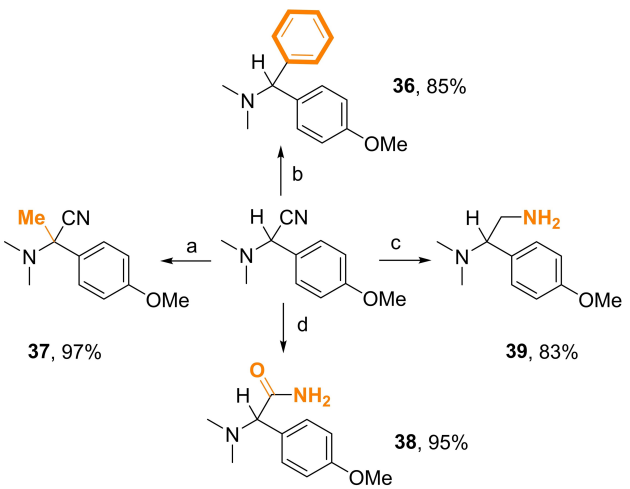
Scheme 2. Postulated mechanism for one-pot synthesis of α-amino nitrile.

Table 1. Optimization of the conditions.



Entry	TMSCN [equiv]	$Ti(OiPr)_4$ [equiv]	R-MgBr[a] [equiv]	Solvent	1/2 ^{1}H NMR Conversion[b]
1	1.2	0.05	1.2	THF	68%/20%
2	1.2	0.15	1.2	THF	88%[c]/–
3	1.2	0.5	1.2	THF	70%[d]/–
4	1.2	–	1.2	THF	54%/34%
5	2.0	0.15	1.2	THF	83%/–
6	1.2	0.15	2.0	THF	86%/–
7	1.2	0.15	1.2	Toluene	72%/–
8	1.2	0.15	1.2	1,4-dioxane	58%/10%
9	1.2	0.15	1.2	MTBE	21%/20%
10	1.2	0.15	1.2	MeTHF	88%/–

[a] 4-methoxyphenyl magnesium bromide (1.0 M in THF). [b] ^{1}H NMR conversion calculated from 1,3,5-trimethoxybenzene as internal standard. [c] 85% Isolated yield.[d] Messy crude.



a/ KHMDS, MeI, THF, 0°C. b/ PhMgBr, THF, reflux. c/ $LiAlH_4$, Et_2O, rt. d/ H_2O_2, K_2CO_3, DMSO, 0°C,

Scheme 3. Modification of the α-amino nitrile function.

Conclusion

We have developed a new synthetic route for the one-pot formation of α-amino nitrile derivatives from *N,N*-dialkyl or unsymmetrically substituted alkylarylformamides. The conditions used herein afford α-amino nitrile derivatives in high yields and offer a complementary access to former protocols since it uses inexpensive, not air-sensitive reagents (Dixon's protocol) or toxic catalyst (Adolfsson's protocol). In addition, our protocol appears suitable for large-scale syntheses. Hence, this methodology constitutes a new opportunity for the synthesis of pharmaceuticals. Investigation regarding the extension of these conditions to amides are currently under investigation in our laboratory.

Experimental Section

General information: All reactions sensitive to moisture and/or air were carried out under argon atmosphere in dry, freshly distilled solvents under anhydrous conditions using oven-dried glassware, unless otherwise noted. THF and toluene were distilled over sodium/benzophenone system, DCM, DMSO and DMF were distilled over calcium hydride, MeOH and EtOH were distilled over magnesium turnings. Reactions were monitored by TLC (silica gel 60 F254plates) and visualization was accomplished with UV light (254 nm & 366 nm) and subsequent use of phosphomolybdic acid solution in EtOH (5%), $KMnO_4$ solution or vanillin/sulfuric acid solution in EtOH, followed by heating at 100–110 °C. Flash chromatography was performed with silica gel 60 (particle size 0.040–0.063 μm). Yield refers to chromatographically and spectroscopically pure compounds, unless otherwise noted. ^{1}H NMR spectra were recorded at 300 and 400 MHz. Chemical shifts are expressed in ppm, relative to the residual ^{1}H solvent signal ($CDCl_3$: δ = 7.26 ppm) as the internal reference. Coupling constants (*J*) are reported in hertz (Hz). The following abbreviations are used to designate the multiplicities: s = singlet; d = doublet; t = triplet; q = quartet; quint. = quintet, sext. = sextet, sept. = septet, m = multiplet; br = broad. ^{1}H NMR assignments were confirmed by 2D COSY spectra. The given multiplicities reflect apparent signal patterns. Diastereomer ratio (*dr*) was estimated by ^{1}H NMR spectroscopic analysis (300, 400 and 600 MHz), unless otherwise noted. ^{13}C NMR spectra were recorded at 75 MHz and 100 MHz. Chemical shifts are given in ppm relative to the residual ^{13}C solvent signal ($CDCl_3$: δ = 77.16 ppm, CD_3OD: δ = 49.00 ppm). ^{13}C NMR assignments were confirmed by 2D HSQC and HMBC spectra. Coupling constants (*J*) are given in Hz for all NMR spectroscopic data. IR spectra were recorded with a FT-IR spectrometer. High-resolution mass spectra (HRMS) were measured on a mass spectrometer equipped with a TOF system and an electrospray ionization (ESI) ion source. Deuterated solvents were used as supplied.

General procedures for condition A and B: To a solution of the respective *N,N*-dialkylformamide (1.25 mmol, 1 eq) in THF (10 mL) was added TMSCN (187.7 μL, 1.5 mmol, 1.2 eq), $Ti(OiPr)_4$ (55.5 μL, 0.18 mmol, 0.15 eq), and after stirring for 10 min, a solution of the respective Grignard reagent (Cond.A: 1.5 mmol, 1.2 eq; Cond.B: 2.5 mmol, 2.0 eq) was added at r.t. The resulting solution was stirred at r.t under air atmosphere and monitored by TLC. Upon completion, 10% aq. NaOH (10 mL) was added. The mixture was filtered, and the filtrate was extracted with DCM (3×20 mL).The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel to give the desired products in a pure form.

General procedure for the reduction reaction: To a solution of the crude (1.0 mmol) from **condition A** or **B** in ether (6 mL) was added to lithium aluminum hydride in small portions over 20 min. The slurry was stirred at R.T. for 12 h. 1 M NaOH (10 mL) was added slowly to quench the reaction. The resulting insoluble material was removed by filtration through Celite, and the filtrate was extracted with ether (3×20 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel to give the desired products in a pure form.

2-(Dimethylamino)-2-(4-methoxyphenyl)acetonitrile (1):[4] Obtained as colorless oil (m = 202.1 mg, 85% yield). Purification by flash chromatography (Diethyl ether/Pentane: 10/90 to 15/85). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.4 Hz, 2H), 6.90 (d, *J* = 8.4 Hz, 2H), 4.77 (s, 1H), 3.82 (s, 3H), 2.31 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 129.1 (2 C), 125.7, 115.3, 114.1 (2 C), 62.5, 55.4, 41.6 (2 C).

2-(Dimethylamino)-2-(p–tolyl)acetonitrile (3):[16] Obtained as yellow solid (m = 191.7 mg, 88% yield). Purification by flash chromatography (Diethyl ether/Pentane: 5/95). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8 Hz, 2H), 7.15 (d, *J* = 8 Hz, 2H), 4.72 (s, 1H), 2.37 (s, 3H), 2.27 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.7, 130.5, 128.7 (2 C), 128.2 (2 C), 115.3, 62.5, 41.6 (2 C), 21.3.

2-(4-Chlorophenyl)-2-(dimethylamino)acetonitrile (4):[16] Obtained as white solid (m = 223.8 mg, 92% yield). Purification by flash chromatography (Diethyl ether/Pentane: 5/95). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 2H), 4.80 (s, 1H), 2.29 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.9, 132.3, 129.2 (2 C), 129.0 (2 C), 114.7, 62.5, 41.7 (2 C).

2-(Dimethylamino)-3-phenylpropanenitrile (5):[17] Obtained as pale yellow oil (m = 182.9 mg, 84% yield). Purification by flash chromatography (Diethyl ether/Pentane: 15/85 to 20/80). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27–7.18 (m, 5H), 3.62 (t, *J* = 8.0 Hz, 1H), 2.94 (d, *J* = 8.0 Hz, 2H), 2.31 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.8, 129.0 (2 C), 128.7 (2 C), 127.3, 116.1, 61.0, 41.8 (2 C), 38.1.

2-Cyclopentyl-2-(dimethylamino)acetonitrile (6): Obtained as colorless oil (m = 138.9 mg, 73% yield). Purification by flash chromatography (Diethyl ether/Pentane: 5/95 to 7/93).^{1}H NMR (400 MHz, $CDCl_3$) δ 3.14 (d, *J* = 10.8 Hz, 1H), 2.29 (s, 6H), 2.25–2.14 (m, 1H), 1.97–1.89 (m, 1H), 1.82–1.74 (m, 1H), 1.66–1.53 (m, 4H), 1.41–1.32 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 116.8, 64.3, 42.0 (2 C), 40.9, 30.7, 29.8, 25.1 (2 C). FTIR (neat): ν = 2955, 1456, 1036, 909, 730 cm^{-1}. HRMS (ESI): *m/z* calcd for $C_9H_{17}N_2$: $[M+H]^+$: 153.1392; found: 153.1387.

2-Cyclohexyl-2-(dimethylamino)acetonitrile (7):[16] Obtained as colorless oil (m = 187.0 mg, 90% yield). Purification by flash chromatography (Diethyl ether/Pentane: 2/98 to 4/96). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.09 (d, *J* = 10.8 Hz, 1H), 2.23 (s, 6H), 2.00–1.89 (m, 2H), 1.80–1.49 (m, 4H), 1.34–1.08 (m, 3H), 1.06–0.73 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 116.2, 65.0, 41.8 (2 C), 38.1, 30.7, 29.6, 26.3, 25.6, 25.4.

2-(Diethylamino)-2-phenylacetonitrile (8):[18] Obtained as yellow oil (m = 214.2 mg, 91% yield). Purification by flash chromatography (Diethyl ether/Pentane: 1/99 to 2/98). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60–7.52 (m, 2H), 7.44–7.32 (m, 3H), 5.02 (s, 1H), 2.68 (dq, *J* = 12.8, 7.2 Hz, 2H), 2.47 (dq, *J* = 12.8, 7.2 Hz, 2H), 1.08 (t, *J* = 7.2 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.6, 128.6 (2 C), 128.5, 127.6 (2 C), 116.3, 58.1, 44.8 (2 C), 13.1 (2 C).

2-(4-Chlorophenyl)-2-(diethylamino)acetonitrile (9):[19] Obtained as yellow oil (m = 200.5 mg, 72% yield). Purification by flash chroma-

tography (Diethyl ether/Pentane: 1/99). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (d, J = 8.5 Hz, 2H), 7.33 (d, J = 8.5 Hz, 2H), 4.95 (s, 1H), 2.62 (dq, J = 13.5, 7.1 Hz, 2H), 2.44 (dp, J = 13.5, 7.1 Hz, 2H), 1.05 (t, J = 7.1 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.4, 133.3, 128.9 (2 C), 128.7 (2 C), 115.9, 57.6, 44.9 (2 C), 13.1 (2 C).

2-(Diethylamino)-2-(4-methoxyphenyl)acetonitrile (10):[20] Obtained as yellow solid (m = 177.3 mg, 65% yield). Purification by flash chromatography (Diethyl ether/Pentane: 2/98 to 3/97). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (d, J = 8.8 Hz, 2H), 6.67 (d, J = 8.8 Hz, 2H), 4.48 (s, 1H), 3.21 (s, 3H), 2.44 (dq, J = 13.2, 7.2 Hz, 2H), 2.25 (dq, J = 13.2, 7.2 Hz, 2H), 0.75 (t, J = 7.2 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.8, 128.9 (2 C), 126.6, 116.7, 114.0 (2 C), 57.6, 55.3, 44.7 (2 C), 13.1 (2 C).

2-(Diethylamino)-3-phenylpropanenitrile (11):[4] Obtained as colorless oil (m = 121.3 mg, 48% yield). Purification by flash chromatography (Diethyl ether/Pentane: 5/95 to 7/93). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40–7.22 (m, 5H), 3.81 (t, J = 7.5 Hz, 1H), 3.03 (d, J = 7.5 Hz, 2H), 2.78 (dq, J = 13.8, 7.0 Hz, 2H), 2.48 (dq, J = 13.8, 7.0 Hz, 2H), 1.09 (t, J = 7.0 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.4, 129.3 (2 C), 128.7 (2 C), 127.3, 118.0, 56.6, 45.4 (2 C), 38.6, 13.3 (2 C).

2-(Dibutylamino)-2-(4-methoxyphenyl)acetonitrile (12): Obtained as white solid (m = 247.0 mg, 72% yield). Purification by flash chromatography (Diethyl ether/Pentane: 2/98). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (d, J = 8.7 Hz, 2H), 6.90 (d, J = 8.7 Hz, 2H), 4.94 (s, 1H), 3.81 (s, 3H), 2.59-2.49 (m, 2H), 2.43–2.35 (m, 2H), 1.45–1.38 (m, 4H), 1.35–1.15 (m, 4H), 0.85 (t, J = 7.2 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 128.9 (2 C), 126.5, 116.4, 113.8 (2 C), 58.1, 55.2, 50.6 (2 C), 29.8 (2 C), 20.2 (2 C), 13.8 (2 C). FTIR (neat): ν = 1510, 1249, 1175, 1034, 908, 729 cm^{-1}. HRMS (ESI): *m/z* calcd for $C_{17}H_{27}N_2O$: $[M+H]^+$: 275.2123; found: 275.2118.

2-(Dibutylamino)-3-phenylpropanenitrile (13):[4] Obtained as colorless oil (m = 226.1 mg, 70% yield). Purification by flash chromatography (Diethyl ether/Pentane: 1/99). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.24 (m, 5H), 3.78 (t, J = 8.0 Hz, 1H), 3.10–2.91 (m, 2H), 2.71–2.60 (m, 2H), 2.48–2.37 (m, 2H), 1.51–1.20 (m, 8H), 0.91 (t, J = 7.4 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.6, 128.6 (2 C), 127.7 (2 C), 125.9, 116.4, 59.4, 50.6 (2 C), 39.5, 29.8 (2 C), 20.2 (2 C), 13.8 (2 C).

2-(Diisopropylamino)-2-phenylacetonitrile (14):[21] Obtained as colorless oil (m = 254.2 mg, 94% yield). Purification by flash chromatography (Diethyl ether/Pentane: 1/99 to 2/98). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56–7.63 (m, 2H), 7.29–7.42 (m, 3H), 4.97 (s, 1H), 3.18 (septet, J = 6.9 Hz, 2H), 1.28 (d, J = 6.9 Hz, 6H), 1.04 (d, J = 6.9 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.6, 128.5 (2 C), 128.2, 127.2 (2 C), 121.0, 50.9, 46.6 (2 C), 23.3 (2 C), 19.4 (2 C).

N1,N1-Diisopropyl-1-(4-methoxyphenyl)ethane-1,2-diamine (15): Obtained as yellow oil (m = 190.9 mg, 61% yield over two steps). Purification by flash chromatography (MeOH/DCM: 2/98 to 6/94). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (d, J = 8.6 Hz, 2H), 6.75 (d, J = 8.6 Hz, 2H), 3.80 (t, J = 7.4 Hz, 1H), 3.70 (s, 3H), 3.60 (br s, 2H), 3.17 (hept, J = 6.8 Hz, 2H), 2.95 (dd, J = 12.8, 7.4 Hz, 1H), 2.79 (dd, J = 12.8, 7.4 Hz, 1H), 1.04 (d, J = 6.8 Hz, 6H), 0.78 (d, J = 6.8 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.3, 133.9, 129.7 (2 C), 113.4 (2 C), 59.1, 55.0, 45.0 (2 C), 43.7, 24.1 (2 C), 21.9 (2 C). FTIR (neat): ν = 2960, 1510, 1247, 1042, 907, 829, 729 cm^{-1}. HRMS (ESI): *m/z* calcd for $C_{15}H_{27}N_2O$: $[M+H]^+$: 251.2123; found: 251.2118.

2-(4-Chlorophenyl)-2-(piperidin-1-yl)acetonitrile (16):[22] Obtained as yellow solid (m = 246.5 mg, 84% yield). Purification by flash chromatography (Diethyl ether/Pentane: 1/99). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 8.5 Hz, 2H), 7.32 (d, J = 8.5 Hz, 2H), 4.75 (s, 1H), 2.45 (t, J = 5.4 Hz, 4H), 1.66–1.38 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.5, 132.2, 129.0 (2 C), 128.7 (2 C), 115.1, 62.2, 50.8 (2 C), 25.7 (2 C), 23.8.

2-(4-Methoxyphenyl)-2-(piperidin-1-yl)acetonitrile (17):[4] Obtained as white solid (m = 210.1 mg, 73% yield). Purification by flash chromatography (Diethyl ether/Pentane: 3/97 to 5/95). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.42 (m, 2H), 6.91–6.89 (m, 2H), 4.75 (s, 1H), 3.81 (s, 3H), 2.53 −2.46 (m, 4H), 1.64–1.45 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 128.9 (2 C), 125.5, 115.7, 113.8 (2 C), 62.3, 55.2, 50.7 (2 C), 25.7 (2 C), 23.9.

3-Phenyl-2-(piperidin-1-yl)propanenitrile (18):[23] Obtained as colorless oil (m = 155.4 mg, 58% yield). Purification by flash chromatography (Diethyl ether/Pentane: 5/95 to 10/90). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19–7.28 (m, 5H), 3.55 (dd, J = 8.0, 8.6 Hz, 1H), 2.95–2.98 (m, 2H), 2.62–2.67 (m, 2H), 2.36–2.41 (m, 2H), 1.44–1.62 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.2, 129.2 (2 C), 128.7 (2 C), 127.3, 116.7, 61.3, 51.1 (2 C), 37.7, 25.8 (2 C), 24.0.

2-Phenyl-2-(piperidin-1-yl)acetonitrile (19):[4] Obtained as yellow oil (m = 182.7 mg, 73% yield). Purification by flash chromatography (Diethyl ether/Pentane: 1/99 to 3/97). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58–7.52 (m, 2H), 7.42–7.34 (m, 3H), 4.81 (s, 1H), 2.56–2.47 (m, 4H), 1.68–1.41 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.6, 128.6, 128.5 (2 C), 127.7 (2 C), 115.5, 62.9, 50.8 (2 C), 25.7 (2 C), 23.9.

2-Cyclopentyl-2-(piperidin-1-yl)acetonitrile (20): Obtained as colorless oil (m = 188.2 mg, 78% yield). Purification by flash chromatography (Diethyl ether/Pentane: 1/99). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.07 (d, J = 10.8 Hz, 1H), 2.61–2.55 (m, 2H), 2.34–2.29 (m, 2H), 2.26–2.21 (m, 1H), 1.93–1.85 (m, 1H), 1.76–1.68 (m, 1H), 1.63–1.49 (m, 9H), 1.45–1.38 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 117.3, 64.1, 51.1 (2 C), 40.3, 30.6, 29.7, 25.8 (2 C), 25.0, 24.9, 24.1. FTIR (neat): ν = 2938, 1453, 1104, 908, 731 cm^{-1}. HRMS (ESI): *m/z* calcd for $C_{12}H_{21}N_2$: $[M+H]^+$: 193.1705; found: 193.1699.

3-Methyl-2-(piperidin-1-yl)butanenitrile (21):[23] Obtained as pale yellow solid (m = 182.8 mg, 88% yield). Purification by flash chromatography (Diethyl ether/Pentane: 1/99 to 2/98). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.93 (d, J = 10.8 Hz, 1H), 2.60–2.53 (m, 2H), 2.37–2.29 (m, 2H), 2.04–1.91 (m, 1H), 1.69–1.53 (m, 4H), 1.51–1.41 (m, 2H), 1.09 (d, J = 6.6 Hz, 3H), 0.98 (d, J = 6.6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 117.2, 66.3, 51.1 (2 C), 28.9, 25.9 (2 C), 24.3, 20.4, 19.3.

2-(Piperidin-1-yl)hexanenitrile (22): Obtained as colorless oil (m = 182.5 mg, 81% yield). Purification by flash chromatography (Diethyl ether/Pentane: 2/98 to 3/97). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.41 (dd, J = 9.0, 6.6 Hz, 1H), 2.65–2.58 (m, 2H), 2.40–2.33 (m, 2H), 1.82–1.31 (m, 12H), 0.91 (t, J = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 117.5, 58.9, 51.0 (2 C), 30.9, 28.3, 25.9 (2 C), 24.2, 22.2, 13.9. FTIR (neat): ν = 2934, 1459, 1168, 1099, 912, 731 cm^{-1}. HRMS (ESI): *m/z* calcd for $C_{11}H_{21}N_2$: $[M+H]^+$: 181.1705; found: 181.1703.

2-(Dibenzylamino)propanenitrile (23):[18] Obtained as white solid (m = 240.9 mg, 77% yield). Purification by flash chromatography (Diethyl ether/Pentane: 1/99). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52–7.08 (m, 10H), 3.96 (d, J = 13.8, 2H), 3.74 (q, J = 7.2, 1H), 3.40 (d, J = 13.8, 2H), 1.48 (d, J = 7.2, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.1 (2 C), 128.8 (4 C), 128.7 (4 C), 127.7 (2 C), 118.2, 55.4 (2 C), 47.8, 18.0.

2-(Dibenzylamino)-3-phenylpropanenitrile (24): Obtained as yellow oil (m = 190.6 mg, 47% yield). Purification by flash chromatography (Diethyl ether/Pentane: 1/99). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.30 (m, 13H), 7.15–7.12 (m, 2H), 4.09 (d, J = 13.6 Hz, 2H), 3.94 (t, J = 8.0 Hz, 1H), 3.53 (d, J = 13.6 Hz, 2H), 3.16 (d, J = 8.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.6 (2 C), 135.7, 129.3 (2 C), 128.6 (5 C), 128.5 (5 C), 127.5 (2 C), 127.2, 117.1, 55.3 (2 C), 54.6, 37.7. FTIR (neat): ν = 1496, 1454, 906, 728, 697 cm^{-1}. HRMS (ESI): *m/z* calcd for $C_{23}H_{23}N_2$: $[M+H]^+$: 327.1861; found: 327.1856.

2-(Dibenzylamino)hexanenitrile (25): Obtained as colorless oil (m = 255.8 mg, 70% yield). Purification by flash chromatography (Diethyl ether/Pentane: 1/99). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.29

(m, 10H), 3.99 (d, J = 13.6 Hz, 2H), 3.60 (t, J = 7.8 Hz, 1H), 3.42 (d, J = 13.6 Hz, 2H), 1.92–1.76 (m, 2H), 1.51–1.32 (m, 2H), 1.29–1.20 (m, 2H), 0.90 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.0 (2 C), 128.8 (4 C), 128.6 (4 C), 127.6 (2 C), 117.7, 55.4 (2 C), 52.8, 31.1, 27.9, 21.9, 13.8. FTIR (neat): ν = 1495, 1459, 908, 730, 697 cm^{-1}. HRMS (ESI): *m/z* calcd for $C_{20}H_{25}N_2$: $[M+H]^+$: 293.2018; found: 293.2015.

2-(Dibenzylamino)-3-methylbutanenitrile (26):[21] Obtained as colorless oil (m = 264.5 mg, 76% yield). Purification by flash chromatography (EtOAc/Cyclohexane : 2/98). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41–7.22 (m, 10H), 3.95 (d, J = 13.6 Hz, 2H), 3.35 (d, J = 13.7 Hz, 2H), 3.08 (d, J = 10.9 Hz, 1H), 2.24–2.00 (m, 1H), 1.03 (t, J = 6.2 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.9 (2 C), 128.9 (4 C), 128.7 (4 C), 127.6 (2 C), 117.2, 55.5 (2 C), 29.2, 20.9, 20.4, 19.5.

N1,N1-Dibenzyl-1-cyclopentylethane-1,2-diamine (27): Obtained as colorless oil (m = 262.2 mg, 68% yield over two steps). Purification by flash chromatography (MeOH/DCM: 2/98 to 3/97). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33–7.20 (m, 10H), 3.82 (d, J = 13.2 Hz, 2H), 3.62 (d, J = 13.2 Hz, 2H), 3.06 (br s, 2H), 2.69–2.59 (m, 2H), 2.49–2.42 (m, 1H), 2.12–2.02 (m, 2H), 1.70–1.53 (m, 5H), 1.39–1.33 (m, 1H), 1.17–1.07 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.1 (2 C), 129.2 (4 C), 128.5 (4 C), 127.2 (2 C), 64.3, 54.5 (2 C), 41.2, 41.0, 32.6, 30.5, 25.2, 24.6. FTIR (neat): ν = 2945, 1456, 1030, 746, 698 cm^{-1}. HRMS (ESI): *m/z* calcd for $C_{21}H_{29}N_2$: $[M+H]^+$: 309.2331; found: 309.2325.

2-(Dibenzylamino)-2-(4-methoxyphenyl)acetonitrile (28):[4] Obtained as yellow oil (m = 231.1 mg, 54% yield). Purification by flash chromatography (Diethyl ether/Pentane: 3/97). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 (d, J = 8.66 Hz, 2H), 7.26–7.13 (m, 10H), 6.78 (d, J = 8.66 Hz, 2H), 4.73 (s, 1H), 3.75 (d, J = 13.35 Hz, 2H), 3.66 (s, 3H), 3.27 (d, J = 13.35 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.8, 137.7 (2 C), 128.8 (4 C), 128.7 (6 C), 128.5 (2 C), 127.5 (2 C), 125.7, 115.6, 114.0, 56.6, 55.2, 54.7.

N1,N1-Dibenzyl-1-(4-chlorophenyl)ethane-1,2-diamine (29): Obtained as yellow oil (m = 228.1 mg, 65% yield over two steps). Purification by flash chromatography (MeOH/DCM: 1/99). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.33 (m, 10H), 7.28–7.25 (m, 2H), 7.20–7.18 (m, 2H), 3.87 (d, J = 13.7 Hz, 2H), 3.71 (dd, J = 8.6, 6.1 Hz, 1H), 3.29 (dd, J = 13.2, 8.6 Hz, 1H), 3.16 (d, J = 13.7 Hz, 2H), 2.89 (dd, J = 13.2, 6.1 Hz, 1H), 1.98 (br s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.6 (2 C), 135.7, 133.4, 130.3 (2 C), 128.8 (4 C), 128.5 (6 C), 127.1 (2 C), 64.5, 54.0 (2 C), 42.7. FTIR (neat): ν = 1493, 1093, 821, 726, 697 cm^{-1}. HRMS (ESI): *m/z* calcd for $C_{22}H_{24}ClN_2$: $[M+H]^+$: 351.1628; found: 351.1623.

2-(4-Methoxyphenyl)-2-(methyl(phenyl)amino)acetonitrile (30):[24] Obtained as white solid (m = 239.7 mg, 76% yield). Purification by flash chromatography (Diethyl ether/Pentane: 5/95). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50–7.48 (m, 2H), 7.39–7.35 (m, 2H), 7.07–6.96 (m, 5H), 5.82 (s, 1H), 3.85 (s, 3H), 2.76 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.9, 148.9, 129.3 (2 C), 128.4 (2 C), 125.1, 120.9, 116.6 (2 C), 116.3,114.2 (2 C), 57.8, 55.2, 34.2.

2-(4-Chlorophenyl)-2-(methyl(phenyl)amino)acetonitrile (31): Obtained as white solid (m = 221.4 mg, 69% yield). Purification by flash chromatography (Diethyl ether/Pentane: 1/99). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53–7.51 (m, 2H), 7.44–7.42 (m, 2H), 7.38–7.33 (m, 2H), 7.06–6.99 (m, 3H), 5.81 (s, 1H), 2.75 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.0, 135.2, 132.1, 129.7 (2 C), 129.4 (2 C), 128.7 (2 C), 121.6, 117.1 (2 C), 115.9, 58.4, 34.9. FTIR (neat): ν = 1598, 1491, 1093, 1015, 906, 728, 692 cm^{-1}. HRMS (ESI): *m/z* calcd for $C_{15}H_{14}ClN_2$: $[M+H]^+$: 257.0846; found: 257.0843.

2-(Methyl(phenyl)amino)-3-phenylpropanenitrile (32): Obtained as colorless oil (m = 180.2 mg, 61% yield). Purification by flash chromatography (Diethyl ether/Pentane: 3/97). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.29 (m, 7H), 6.99–6.95 (m, 1H), 6.91–6.89 (m, 2H), 4.69 (t, J = 7.6 Hz, 1H), 3.21 (d, J = 7.6 Hz, 2H), 3.01 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.0, 135.4, 129.4 (2 C), 129.3 (2 C), 128.9 (2 C), 127.6, 121.0, 117.5, 116.8 (2 C), 56.7, 38.1, 34.8. FTIR (neat): ν = 1599, 1497, 905, 725, 696 cm^{-1}. HRMS (ESI): *m/z* calcd for $C_{16}H_{17}N_2$: $[M+H]^+$: 237.1392; found: 237.1387.

2-(Methyl(phenyl)amino)propanenitrile (33):[25] Obtained as yellow oil (m = 81.2 mg, 41% yield). Purification by flash chromatography (Diethyl ether/Pentane: 2/98). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (t, J = 8.0 Hz, 2H), 6.96-6.93 (m, 3H), 4.62 (q, J = 7.5 Hz, 1H), 2.90 (s, 3H), 1.59 (d, J = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.1, 129.5 (2 C), 121.3, 118.6, 117.2 (2 C), 49.2, 34.5, 18.1.

2-(methyl(phenyl)amino)hexanenitrile (34):[26] Obtained as yellow oil (m = 194.7 mg, 77% yield). Purification by flash chromatography (Diethyl ether/Pentane: 1/99). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39–7.25 (m, 2H), 7.02–6.88 (m, 3H), 4.46 (t, J = 7.9 Hz, 1H), 2.90 (s, 3H), 2.02–1.85 (m, 2H), 1.57–1.33 (m, 4H), 0.95 (t, J = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.5, 129.5 (2 C), 120.9, 118.2, 116.7 (2 C), 54.2, 34.3, 31.6, 28.0, 22.2, 14.0.

3-Methyl-2-(methyl(phenyl)amino)butanenitrile (35):[27] Obtained as yellow oil (m = 202.4 mg, 86% yield). Purification by flash chromatography (Diethyl ether/Pentane: 1/99 to 2/98). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28–7.37 (m, 2H), 6.89–7.00 (m, 3H), 4.05 (d, J = 10.6 Hz, 1H), 2.91 (s, 3H), 2.17–2.33 (m, 1H), 1.22 (d, J = 6.6 Hz, 3H), 1.07 (d, J = 6.6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.6, 129.3 (2 C), 120.5, 117.4, 116.3 (2 C), 61.4, 34.2, 30.4, 19.7, 18.9.

Detailed procedure for the synthesis of 36: To a solution of compound **1** (190 mg, 1.0 mmol) in THF (5 mL) was added 1 M solution of PhMgBr (3.0 mmol) in THF. The mixture was fluxed overnight and quenched with 1 M aqueous HCl. Then, THF was removed under reduced pressure. NaOH was added to neutralize the solution followed by extraction with DCM (10 mL × 3). The organic phase was dried over $MgSO_4$, and concentrated under reduced pressure. 205.1 mg (85% yield) of compound **36** were obtained as colorless oil after purification by flash column chromatography on silical gel (EtOAc/Cyclohexane: 2/98 to 5/95).

1-(4-Methoxyphenyl)-N,N-dimethyl-1-phenylmethanamine (36):[28] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 (d, J = 8.1 Hz, 2H), 7.24–7.34 (m, 4H), 7.14–7.18 (m, 1H), 6.81 (d, J = 8.1 Hz, 2H), 4.02 (s, 1H), 3.74 (s, 3H), 2.18 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.5, 143.4, 135.6, 128.8 (2 C), 128.5 (2 C), 127.6 (2 C), 126.8, 113.8 (2 C), 77.3, 55.2, 44.7 (2 C).

Detailed procedure for the synthesis of 37: To a solution of compound **1** (190 mg, 1.0 mmol) in dry THF (3 mL) under Ar atmosphere was added a 0.7 M solution of KHMDS in toluene (1.4 mL, 1.0 mmol) dropwise at 0 °C and the solution was stirred for 20 min. MeI (77.8 μL, 1.25 mmol) was then added dropwise and, after 10 min, 5 mLof saturaed NH_4Cl aqueous solution was added to quench the reaction. The reaction mixture was extracted with Et_2O (8 mL × 3), dried over $MgSO_4$, and concentrated under reduced pressure. 198.1 mg (97% yield) of compound **37** were obtained as colorless oil after purification by flash column chromatography on silical gel (EtOAc/Cyclohexane: 2/98)

2-(Dimethylamino)-2-(4-methoxyphenyl)propanenitrile (37): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, J = 8.9 Hz, 2H), 6.88 (d, J = 8.9 Hz, 2H), 3.80 (s, 3H), 2.26 (s, 6H), 1.69 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 133.2, 126.8 (2 C), 118.0, 114.1 (2 C), 66.8, 55.4, 40.9 (2 C), 29.4. FTIR (neat): ν = 1509, 1248, 1177, 1036, 913, 838, 730 cm^{-1}. HRMS (ESI): *m/z* calcd for $C_{12}H_{17}N_2O$: $[M+H]^+$: 205.1341; found: 205.1340.

Detailed procedure for the Synthesis of 38: To a solution of compound **1** (190 mg, 1.0 mmol) in DMSO (2 mL) was added K_2CO_3 (40 mg) and the mixture cooled in an ice bath. H_2O_2 solution (30%,

0.5 mL) was then added dropwise, resulting in an exothermic reaction. After stirring and cooling for further 10 min, the reaction was quenched by H_2O (10 mL). The reaction mixture was extracted with DCM (10 mL×3), dried over $MgSO_4$, and concentrated under reduced pressure. 197.8 mg (95% yield) of compound **38** were obtained as white solid after purification by flash column chromatography on silical gel (MeOH/DCM: 2/98 to 5/95).

2-(Dimethylamino)-2-(4-methoxyphenyl)acetamide (38): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28–7.23 (m, 2H), 6.96 (br s, 1H), 6.88–6.84 (m, 2H), 6.01 (br s, 1H), 3.79 (s, 3H), 3.66 (s, 1H), 2.20 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 159.6, 130.0 (2 C), 128.5, 114.0 (2 C), 76.4, 55.4, 43.9 (2 C). FTIR (neat): ν=1738, 1664, 1513, 1366, 1027, 823, 731 cm^{-1}. HRMS (ESI): *m/z* calcd for $C_{11}H_{17}N_2O_2$: $[M+H]^+$: 209.1290; found: 209.1285.

1-(4-Methoxyphenyl)-N1,N1-dimethylethane-1,2-diamine (39): Obtained as yellow oil (m=161.2 mg, 83% yield). Purification by flash chromatography (MeOH/DCM: 0/100 to 20/80). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.15 (d, J=8.7 Hz, 2H), 6.86 (d, J=8.7 Hz, 2H), 3.79 (s, 3H), 3.13 (q, J=6.0 Hz, 1H), 3.06 (t, J=6.2 Hz, 1H), 2.94–2.88 (m, 1H), 2.16 (s, 6H), 1.41 (br s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 130.8, 129.7 (2 C), 113.6 (2 C), 72.1, 55.2, 44.3, 42.7 (2 C). FTIR (neat): ν=1513, 1245, 1039, 907, 829, 727 cm^{-1}. HRMS (ESI): *m/z* calcd for $C_{11}H_{19}N_2O$: $[M+H]^+$: 195.1497; found: 195.1494.

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Conflict of Interest

The authors declare no conflict of interest.

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