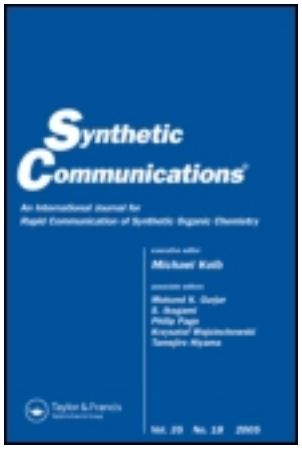

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Basic Ionic Liquid as Catalyst for the Efficient and Green Synthesis of 2-Amino-3-nitrobenzonitriles in Ethanol

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BASIC IONIC LIQUID AS CATALYST FOR THE EFFICIENT AND GREEN SYNTHESIS OF 2-AMINO-3-NITROBENZONITRILES IN ETHANOL

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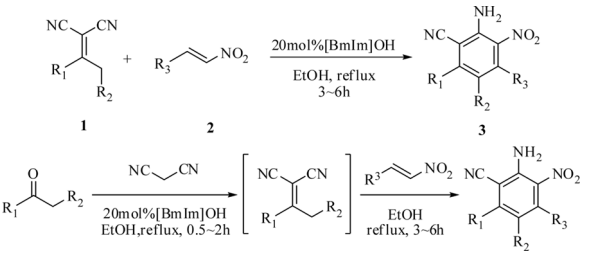
GRAPHICAL ABSTRACT



Abstract *A basic ionic liquid, [BmIm]OH was used as catalyst in the cyclocondensation of various kinds of vinylmalononitriles with nitroolefins in ethanol at reflux. A series of 2-amino-3-nitrobenzonitriles were obtained in reasonable yields. The straightforward and green protocol was found to be fairly efficient, and the catalyst could be recycled and reused in subsequent reactions with consistent activity. The mechanism of the reaction was discussed.*

Keywords 2-Amino-3-nitrobenzonitriles; catalyze; ionic liquid; vinylmalononitrile

Polysubstituted benzenes are important compounds in organic and natural product chemistry. Likewise, as common structural units and frequently employed synthetic precursors of many bioactive compounds,[1] they also play important roles in medicinal chemistry.

Generally, using traditional routes of aromatic substitutions, such as Friedel–Crafts reactions,[2] nucleophilic substitutions,[3] or coupling reactions,[4] it is difficult to introduce amino and/or nitrile groups to given aromatics. Fortunately, some methods have been developed to synthesize these multifunctionalized benzenes from acyclic precursors using vinylmalononitriles as key starting materials.[5] However,

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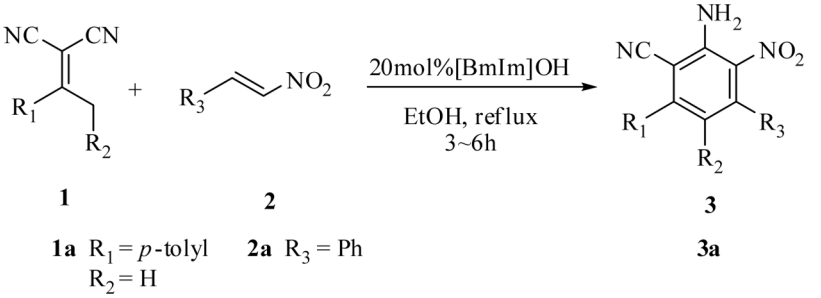
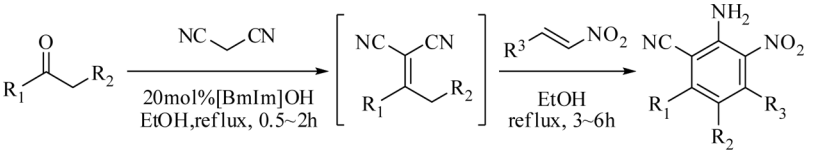


Scheme 1. Synthetic protocol for 2-amino-3-nitrobenzonitriles.

these methods often suffer from certain drawbacks such as long procedures, hazardous by-products, and use of equivalent or even excess amounts of alkali. Therefore, how to synthesize polysubstituted benzenes efficiently and cleanly remains a necessary problem to solve.

Ionic liquids, because of their unique properties such as noninflammability, negligible vapor pressure, reusability, and high thermal stability,[6] have attracted extensive research interest in the area of green chemistry in recent years. Moreover, a task-specific basic ionic liquid, [BmIm]OH, has been successfully applied as a catalyst to perform several classical organic reactions[7] and the synthesis of substituted heterocycles such as pyrrole[8] and pyridine.[9] Recently, our group has reported a simple and efficient synthetic protocol for polysubstituted benzenes using $Cu(OTf)_2/Et_3N$ as a novel catalytic system in CH_3CN.[10] As part of our ongoing interest in green chemistry, in this article, we introduce [BmIm]OH as a mild, highly efficient, and environmentally benign catalyst for the preparation of substituted 2-amino-3-nitrobenzonitriles (Scheme 1). Additionally, one-pot synthesis of 2-amino-3-nitrobenzonitriles was achieved via Knoevenagel condensation of ketone with malononitrile and a sequential tandem reaction with nitroolefins (Scheme 2).

At the onset of this work, we investigated the appropriate loading amounts of catalyst and selected the solvent with the model reaction of **1a** with **2a** using [BmIm]OH as catalyst. The results are summarized in Table 1. It was found that 20 mol% of [BmIm]OH was enough to promote the reaction efficiently and the catalyst could be reused three times without evident loss of activity (Table 1, entry 3). We expected the reaction to perform in aqueous media, but probably as a result of the poor solubility of the two starting materials in water, the result was disappointing (Table 1, entry 6, 48%). Moreover, the solvent-free condition was also examined, and a viscous reaction system and moderate yield were found (Table 1, entry 7,



Scheme 2. One-pot synthesis of 2-amino-3-nitrobenzonitriles from ketones.

Table 1. Reaction of **1a** and **2a** under different conditions[a]

Entry	[BmIm]OH (mol%)	Solvent	Yield (%)[b]
1	10	EtOH	67
2	15	EtOH	79
3	20	EtOH	86, 79, 81[c]
4	50	EtOH	82
5	100	EtOH	81
6	20	H_2O	48
7	20	—	67
8	—	[BmIm]OH	80

[a]The reaction was carried out at 80 °C or reflux for 4 h.
[b]Yield of isolated product.
[c][BmIm]OH was reused three times.

67%). EtOH was a better solvent (Table 1, entry 3, yield 86%) than other solvents tested.

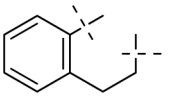
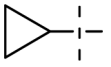
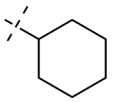
The subsequent study was performed under the optimized conditions: with 20 mol% [BmIm]OH in ethanol at reflux, as described in Scheme 1. Most of the corresponding products, substituted 2-amino-3-nitrobenzonitriles **3**, were obtained in good yields.

It was observed the process tolerated both electron-donating and electron-withdrawing groups on phenyl when a series of substituted phenylethylidenemalononitriles (Table 2, entries 1–7) were used to react with **2a**. When phenyl was replaced with furan-2-yl, the corresponding product was obtained in good yield (Table 2, entry 8, 86% yield). We also attempted to use vinylmalononitriles with aliphatic R^1 and R^2 to perform the reactions with **2a**, which similarly gave the corresponding products in satisfying yields (Table 2, entries 9–12). A cyclopropylbenzene framework, which was difficult to prepare via aromatic subsitution, was constructed expediently. Presumably as a result of steric hindrance, indeed, no reaction of 2-(2-phenyl-1-p-tolylethylidene)malononitrile with **2a** was observed under the same conditions (Table 2, entry 15). Furthermore, a wide range of nitroolefins with different R^3 was reacted with 2-(1-phenylethylidene)malononitrile. Similar yields were obtained irrespective of R^3 being substituted phenyl, alkyl, and heterocycle (Table 2, entries 16–21).

It was reported [BmIm]OH provides an efficient and convenient methodology for the Knoevenagel condensation reaction between ketone and malononitrile.[7j] The report inspired us to apply the one-pot strategy for the synthesis of 2-amino-3-nitrobenzonitriles using ketones as starting materials (Scheme 2). As expectation, catalyzed by [BmIm]OH in a minimum amount of EtOH at reflux, many ketones reacted with malononitrile rapidly and afforded the corresponding vinylmalononitriles completely (monitored by thin-layer chromatography, TLC). Without further purification, nitroolefins were then added to the reaction system to accomplish the subsequent cyclocondensation. The products were obtained in moderate to good yields based on ketones, as shown in the parentheses in Table 2.

In the reaction of **1a** and **2a** catalyzed by [BmIm]OH in EtOH, after stirring for 8 h at room temperature, the important intermediate, 2-(4-nitro-3-phenyl-1-p-tolylbutylidene)malononitrile **4a**, was obtained (Scheme 3) in 90% yield. It suggested that

Table 2. [BmIm]OH-promoted synthesis of 2-amino-3-nitro benzonitriles in EtOH at reflux[a]

Entry	R_1	R_2	R_3	Time (h)[b]	Product	Yield (%)[c]
1	4-MeC_6H_4	H	Ph	4 (5.5)	**3a**	86 (74)
2	Ph	H	Ph	4 (5.5)	**3b**	84 (73)
3	4-$MeOC_6H_4$	H	Ph	3.5 (4.5)	**3c**	88 (77)
4	4-FC_6H_4	H	Ph	5	**3d**	79
5	4-ClC_6H_4	H	Ph	4.5	**3e**	86
6	3-ClC_6H_4	H	Ph	5	**3f**	76
7	3,4-$(MeO)_2C_6H_3$	H	Ph	3 (4.5)	**3g**	84 (72)
8	furan-2-yl	H	Ph	3 (4)	**3h**	86 (75)
9			Ph	4 (6)	**3i**	82 (70)
10			Ph	4 (4.5)	**3j**	81 (72)
11			Ph	4 (4.5)	**3k**	81 (73)
12		H	Ph	4.5 (5.5)	**3l**	80 (68)
13	Ph	Me	Ph	5	**3m**	72
14	3-ClC_6H_4	Me	Ph	5.5	**3n**	64
15	4-MeC_6H_4	Ph	Ph	6	**/**	0
16	Ph	H	furan-2-yl	4 (5.5)	**3o**	85 (73)
17	Ph	H	thien-2-yl	4 (5.5)	**3p**	84 (70)
18	Ph	H	4-$MeOC_6H_4$	4 (5.5)	**3q**	85 (71)
19	Ph	H	3-$MeOC_6H_4$	4 (5.5)	**3r**	83 (68)
20	Ph	H	3-$NO_2C_6H_4$	4 (5.5)	**3s**	82 (70)
21	Ph	H		4 (5.5)	**3t**	84 (72)

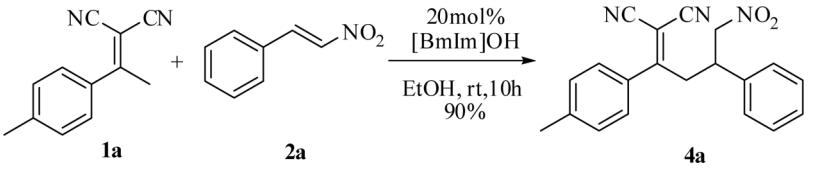
[a]All reactions were carried out on a 1 mmol vinylmalononitriles with 1 mmol nitroolefins in the presence of 0.2 mmol [BmIm]OH in EtOH (3 mL) at reflux.

[b]Reaction time of one-pot synthesis of 2-amino-3-nitro benzonitriles from ketones (in bracket).

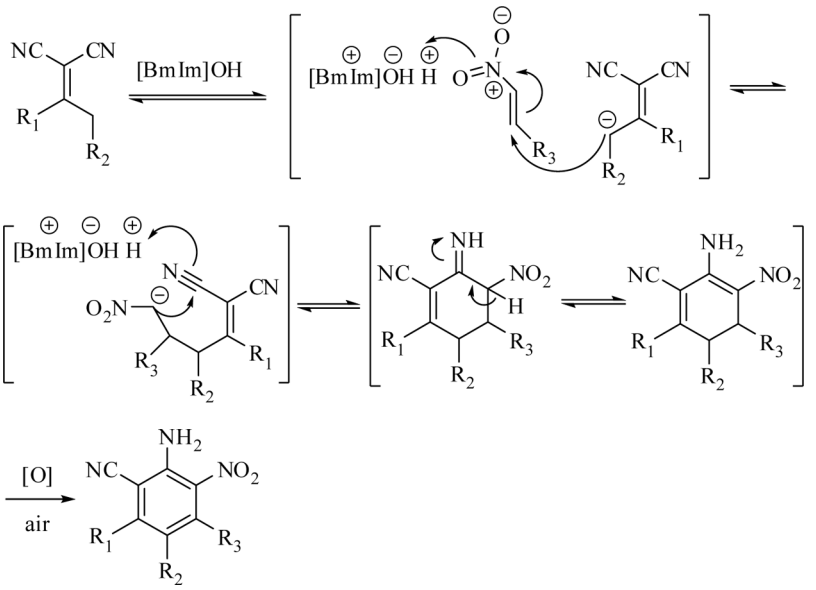
[c]Isolated yields based on vinylmalononitrles and yields of one-pot synthesis of 2-amino-3-nitro benzonitriles based on ketones (in bracket).

the reaction pass through an ionic mechanism. With all these results in hand, we propose a plausible mechanism for [BmIm]OH catalyzed synthesis of 2-amino-3-nitrobenzonitriles in Scheme 4.

In summary, a new catalytic protocol to synthesize 2-amino-3-nitrobenzonitriles via the cyclocondensation of various vinylmalonitriles and nitroolefins has been



Scheme 3. Preparation of important intermediate **4a**.



Scheme 4. Plausible mechanism.

developed. [BmIm]OH was efficient to promote a one-pot synthesis of 2-amino-3-nitrobenzonitriles via Knoveangal condensation reaction of ketone and malononitrile and a sequential tandem reaction with nitroolefins. Compared with previously reported methodelogies, the attractive features of the present process are simple workup, short reaction time, environmentally benign solvent, reusability of basic ionic [BmIm]OH, and its adaptability for the synthesis of a broad range of polysubstituted 2-amino-3-nitrobenzonitriles in good yields.

EXPERIMENTAL

Melting points are uncorrected. ^{1}HNMR and ^{13}CNMR spectra were recorded on Varian 400 or 500 instruments using tetramethylsilane (TMS) as internal standard. Mass spectroscopy (MS) data of the products were collected on a MS–EI instrument (Finnigan Trace DSQ). Infrared (IR) spectra were collected on a Nicolet 2100 IR spectrometer. All reactions were monitored by TLC with GF254 silica-gel-coated plates. Starting materials and solvents were purchased from common commercial sources or prepared via common method without further purification.

The reaction mixture was purified by column chromatography over silica gel (200–300 mesh). The synthesis of this basic ionic liquid was prepared as previously described.[7f]

Typical Procedure for the Preparation of 2-Amino-3-nitrobenzonitriles

Vinylmalononitile (1 mmol), nitroolefin (1 mmol), and [BmIm]OH (0.2 mmol, 18 mg) were dissolved in a minimum amount (1 mL) of ethanol to carry out the reaction in a solution phase. The reaction mixture was stirred at reflux temperature for the desired time. After the completion of the reaction (monitored by TLC), EtOAc (15 mL) was added to dilute the reaction solution. Then the mixture was washed with water. The combined organic phases were dried and concentrated in vacuo, purified by column chromatography [silica gel, hexane/AcOEt (v/v) = 8:1] to afford the 2-amino-3-nitrobenzonitrile **3**. The products could be easily identified by the singlet peak of the amido in ^{1}H NMR spectra. The residue aqueous phase was evaporated under reduced pressure, and the remaining [BmIm]OH was rinsed with ethyl acetate, dried under a vacuum, and reused for three runs.

Typical Procedure for the One-Pot Synthesis of 2-Amino-3-nitrobenzonitriles from Ketones

A minimum amount (1 mL) of ethanol was added to a mixture of ketone (1 mmol), malononitrile (1 mmol), and [BmIm]OH (0.2 mmol, 18 mg) to carry out the reaction in a solution phase. The reaction mixture was stirred at reflux temperature and monitored by TLC. When vinylmalononitrile was obtained completely, without further purification, nitroolefins (1 mmol) were then added to the reaction system and stirred for the desired time to accomplish the subsequent cyclocondensation. After the completion of the reaction (monitored by TLC), EtOAc (15 mL) was added to dilute the reaction solution. Then the mixture was washed with water. The combined organic phases were dried and concentrated in vacuo and purified by column chromatography [silica gel, hexane/AcOEt (v/v) = 8:1] to afford the 2-amino-3-nitrobenzonitrile 3.

Selected Data

Compound 3a. Yellow crystals; mp 196–198 °C; yield: 86%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.49 (5H, m, Ar*H*), 7.26–7.34 (4H, m, Ar*H*), 6.80 (1H, s, Ar*H*), 5.88 (2H, s, NH_2), 2.43 (3H, s, CH_3). MS (EI): m/z (%) = 330 (35, $M^+ + 1$), 329 (M^+, 100). HRMS (EI) calcd. for $C_{20}H_{15}N_3O_2$ ($[M]^+$) 329.1164; found: 329.1162.

Compound 3b. Mp 202–203 °C (lit.[5a] 204.2–205.8 °C); yield: 84% (lit.[5a] 76%). ^{1}HNMR (500 MHz, $CDCl_3$) δ 7.57–7.59 (2H, m, Ar*H*), 7.50 (2H, dd, $J_1$2.0 Hz, J_2 5.5 Hz, Ar*H*), 7.43 (3H, dd, $J_1$2.0 Hz, J_2 5.5 Hz, Ar*H*), 7.32–7.34 (2H, m, Ar*H*), 6.81 (1H, s, Ar*H*), 5.87 (2H, s, NH_2). ^{13}CNMR (125 MHz, $CDCl_3$) δ

149.5, 144.8, 143.0, 137.3, 137.0, 130.0, 129.0, 128.4, 127.2, 115.8, 97.7. MS (EI): m/z (%) = 315 (M^+, 52), 77 (100).

Compound 3c. Yellow crystals; mp 191–192 °C; yield: 88%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (2H, dd, J_1 2.0 Hz, J_2 6.8 Hz, Ar*H*), 7.43–7.45 (3H, m, Ar*H*), 7.32–7.34 (2H, m, Ar*H*), 7.02 (2H, dd, J_1 2.0 Hz, J_2 6.8 Hz, Ar*H*), 6.78 (1H, s, Ar*H*), 5.91 (2H, s, NH_2), 3.87 (3H, s, OCH_3). ^{13}CNMR (125 MHz, $CDCl_3$) δ 161.0, 149.3, 145.0, 143.0, 137.5, 133.7, 129.9, 129.2, 128.9, 128.8, 127.2, 126.3, 121.1, 116.2, 114.4, 92.3, 55.4. MS (EI) m/z (%) = 345 (M^+, 44), 114 (100). HRMS (EI) calcd. for $C_{20}H_{15}N_3O_3$ ([M]$^+$) 345.1113; found: 345.1112.

Compound 3d. Yellow crystals; mp 193–194 °C; yield: 79%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56–7.59 (2H, m, Ar*H*), 7.43 (3H, dd, J_1 4.0 Hz, J_2 6.0 Hz, Ar*H*), 7.33 (2H, dd, J_1 2.5 Hz, J_2 6.0 Hz, Ar*H*), 7.21 (2H, q, J 9.0 Hz, Ar*H*), 6.77 (1H, s, Ar*H*), 5.87 (2H, s, NH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.8 (J 311 Hz), 148.4, 144.8, 143.1, 137.2, 134.4, 129.0, 127.2, 121.1, 116.2, 116.0, 115.7, 97.7. IR (KBr) ν_{max}: 3481, 3373, 2216, 1502, 1280, 837, 770. MS (EI) m/z (%) = 334 ($M^+ + 1$, 7), 333 (M^+, 30), 59 (100). HRMS (EI) calcd. for $C_{19}H_{12}FN_3O_2$ ([M]$^+$) 333.0914; found: 333.0915.

Compound 3e. Yellow crystals; mp 183–184 °C; yield: 82%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47–7.53 (4H, m, Ar*H*), 7.42–7.45 (3H, m, Ar*H*), 7.31–7.33 (2H, m, Ar*H*), 6.77 (1H, s, Ar*H*), 5.86 (2H, s, NH_2). ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.1, 144.8, 143.1, 137.1, 136.2, 135.4, 134.5, 129.8, 129.2, 129.0, 128.9, 127.2, 121.0, 115.6, 97.6. IR (KBr) ν_{max}: 3467, 3354, 2217, 1497, 1097. MS (EI) m/z (%) = 349 (M^+, 100). HRMS (EI) calcd. for $C_{19}H_{12}ClN_3O_2$ ([M]$^+$) 349.0618; found: 349.0619.

Compound 3f. Yellow crystals; mp 180–181 °C; yield: 76%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (1H, d, J 1.6 Hz, Ar*H*), 7.44–7.51 (6H, m, Ar*H*), 7.32–7.34 (2H, m, Ar*H*), 6.79 (1H, s, Ar*H*), 5.86 (2H, s, NH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.2, 145.9, 143.9, 138.1, 137.2, 135.0, 134.5, 128.6, 129.5, 129.0 (2C), 127.2, 121.6, 116.1, 98.2. IR (KBr) ν_{max}: 3511, 3372, 2224, 1505, 1088. MS (EI) m/z (%) = 349 (M^+, 100). HRMS (EI) calcd. for $C_{19}H_{12}ClN_3O_2$ ([M]$^+$) 349.0618; found: 349.0615.

Compound 3g. Yellow crystals; mp 176–177 °C; yield: 84%. ^{1}H NMR (400 MHz, $CDCl_3$) 7.43–7.45 (3H, m, Ar*H*), 7.34 (1H, t, J 3.6 Hz, Ar*H*), 7.32 (1H, s, Ar*H*), 7.19 (1H, dd, J_1 2.0 Hz, J_2 8.4 Hz, Ar*H*), 7.11 (1H, d, J 3.0 Hz, Ar*H*), 6.98 (1H, d, J 3.0 Hz, Ar*H*), 6.81 (1H, s, Ar*H*), 5.90 (2H, s, NH_2), 3.95 (6H, s, OCH_3). ^{13}CNMR (100 Hz, $CDCl_3$) δ 150.6, 149.3, 149.2, 145.0, 143.0, 137.5, 133.8, 129.5, 128.9 (2C), 127.2, 121.5, 121.0, 116.1, 111.6, 111.4, 97.4, 56.1, 56.0. MS (EI) m/z (%) = 376 ($M^+ + 1$, 19), 375 (M^+, 100). HRMS (EI) calcd. for $C_{21}H_{17}N_3O_4$ ([M]$^+$) 375.1219; found: 375.1213.

3-Amino-5-(furan-2-yl)-2-nitrobiphenyl-4-carbonitrile (3h). Yellow crystals; mp 188–189 °C (lit.[5a] 188.4–191.2 °C); yield: 86% (lit.[5a] 67%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (1H, s, Ar*H*), 7.44 (4H, t, J 2.5 Hz, Ar*H*), 7.33–7.34 (2H, t, Ar*H*), 7.20 (1H, s, Ar*H*), 6.61 (1H, d, J 1 Hz, Ar*H*), 5.96 (2H, s, NH_2). ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.7, 145.4, 144.9, 143.5, 137.6, 136.2, 133.3,

128.9, 128.8, 127.1, 117.1, 116.2, 113.4, 113.0. MS (EI) m/z (%) = 306 ($M^+ + 1$, 30), 305 (M^+, 100). IR (KBr) ν_{max}: 3467, 3363, 2212, 1571, 1553, 1494, 1483, 759. HRMS (EI) calcd. for $C_{17}H_{11}N_3O_3$ ($[M]^+$) 305.0800; found: 305.0802.

3-Amino-2-nitro-1-phenyl-9,10-dihydrophenanthrene-4-carbonitrile (3i). Yellow crystals; mp 201–202 °C (lit.[5a] 201.2–203.4 °C); yield: 82% (lit.[5a] 71%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (1H, t, J 2.0 Hz, ArH), 7.40–7.47 (5H, m, ArH), 7.28 (1H, dd, J_1 6.5 Hz, J_2 8.5 Hz, ArH), 7.20–7.22 (2H, m, ArH), 5.66 (2H, s, NH_2), 2.64 (2H, q, J 5.0 Hz, CH_2CH$_2$), 2.39 (2H, q, J 5.0 Hz, CH$_2$CH_2). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.3, 142.5, 140.4, 139.8, 135.7, 131.1, 130.5, 128.8, 128.6, 128.0, 127.9, 127.4, 127.1, 117.2, 95.4, 29.1, 26.0. IR (KBr) ν_{max}: 3466, 3382, 2214, 1620, 1512, 920, 706. MS (EI) m/z (%) = 341 (M^+, 54), 305 (100).

2-Amino-3-nitro-4-phenyl-5,6,7,8-tetrahydronaphthalene-1-carbonitrile (3j). Mp 209–210 °C (lit.[5a] 211.2–214.3 °C); yield: 81% (lit.[5a] 62%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37–7.43 (3H, m, ArH), 7.14 (2H, d, J 7.5 Hz, ArH), 5.35 (2H, s, NH_2), 2.96 (2H, t, J 7.5 Hz, CH_2), 2.23 (2H, t, J 7.5 Hz, CH_2), 1.77–1.82 (2H, m, CH_2), 1.62–1.67 (2H, m, CH_2). IR (KBr) ν_{max}: 3463, 3357, 2940, 2220, 1518. MS (EI) m/z (%) = 294 ($M^+ + 1$, 15), 293 (M^+, 100).

5-Amino-6-nitro-7-phenyl-2,3-dihydro-1H-indene-4-carbonitrile (3k). Yellow crystals; mp 197–198 °C; yield: 81%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.44 (3H, m, ArH), 7.18–7.21 (2H, m, ArH), 5.61 (2H, s, NH_2), 3.12 (2H, t, J 3.6 Hz, CH_2), 2.65 (2H, t, J 3.6 Hz, CH_2), 2.05–2.12 (2H, m, CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8, 143.1, 138.8, 136.3, 133.9, 128.7, 128.3, 127.2, 115.1, 95.4, 33.9, 32.0, 29.7. IR (KBr) ν_{max}: 3475, 3362, 2923, 2220, 1513. MS (EI) m/z (%) = 280 ($M^+ + 1$, 18), 279 (M^+, 100). HRMS (EI) calcd. for $C_{16}H_{13}N_3O_2$ ($[M]^+$) 279.1008; found: 279.1012.

3-Amino-5-cyclopropyl-2-nitrobiphenyl-4-carbonitrile (3l). Yellow crystals; mp 164–165 °C; yield: 81%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40–7.42 (3H, m, ArH), 7.23–7.26 (2H, m, ArH), 6.12 (1H, s, ArH), 5.85 (2H, s, NH_2), 2.24–2.29 (1H, m, CH), 1.21–1.25 (2H, m, CH_2), 0.88–0.91 (2H, m, CH_2). ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.7, 144.4, 143.5, 138.0, 128.9, 127.1, 115.3, 115.2, 99.3, 15.1, 10.8. MS (EI) m/z (%) = 280 ($M^+ + 1$, 18), 279 (M^+, 100). HRMS (EI) calcd. for $C_{16}H_{13}N_3O_2$ ($[M]^+$) 279.1008; found: 279.1010.

Compound 3m. Yellow crystals; mp 171–172 °C; yield: 72%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39–7.52 (6H, m, ArH), 7.29–7.31 (2H, m, ArH), 7.21–7.23 (2H, m, ArH), 5.36 (2H, s, NH_2), 1.71 (3H, s, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.6, 141.7, 141.1, 137.4, 138.6, 136.0, 129.0, 128.9, 128.7, 128.5, 128.1, 125.6, 115.5, 100.8, 17.9. MS (EI) m/z (%) = 330 ($M^+ + 1$, 22), 329 (M^+, 100). HRMS (EI) calcd. for $C_{20}H_{15}N_3O_2$ ($[M]^+$) 329.1164; found: 329.1169.

Compound 3n. Yellow crystals; mp 164–165 °C; yield: 64%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41–7.46 (5H, m, ArH), 7.31 (1H, d, J 0.5 Hz, ArH), 7.19–7.22 (3H, m, ArH), 5.36 (2H, s, NH_2), 1.72 (3H, s, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.8, 141.9, 139.1, 137.1, 135.6, 134.9, 130.3, 129.3, 128.8, 128.1, 127.9, 126.7, 125.5, 115.2, 110.0, 59.5. IR (KBr) ν_{max}: 3463, 3353, 2223,

1513. MS (EI) m/z (%) = 363 (M^+, 18), 94 (100). HRMS (EI) calcd. for $C_{20}H_{14}ClN_3O_2$ ([M]$^+$) 363.0775; found: 363.0773.

3-Amino-5-(furan-2-yl)-4-nitrobiphenyl-2-carbonitrile (3o). Yellow crystals; mp 164–165 °C; yield: 85%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50–7.58 (5H, m, Ar*H*), 7.26 (1H, s, Ar*H*), 7.05 (1H, s, Ar*H*), 6.76 (1H, d, *J* 3.2 Hz, Ar*H*), 6.53 (1H, dd, J_1 2.0 Hz, J_2 3.2 Hz, Ar*H*), 6.58 (2H, s, NH_2). ^{13}C NMR (125 MHz, $CDCl_3$) δ 117.0, 110.7, 107.3, 106.7, 99.5, 92.3, 92.1, 90.9, 80.5, 78.2, 74.8, 74.1. MS (EI) m/z (%) = 305 (M^+, 23), 232 (100). HRMS (EI) calcd. for $C_{17}H_{11}N_3O_3$ ([M]$^+$) 305.0800; found: 305.0801.

3-Amino-4-nitro-5-(thiophen-2-yl)biphenyl-2-carbonitrile (3p). Yellow crystals; mp 171–172 °C; yield: 84%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56–7.58 (2H, m, Ar*H*), 7.50–7.53 (3H, m, Ar*H*), 7.46 (1H, dd, J_1 2.0 Hz, J_2 5.0 Hz, Ar*H*), 7.08–7.13 (2H, m, Ar*H*), 6.92 (1H, s, Ar*H*), 5.65 (2H, s, NH_2). MS (EI) m/z (%) = 322 ($M^+ + 1$, 23), 321 (M^+, 100). HRMS (EI) calcd. for $C_{17}H_{11}N_3O_2S$ ([M]$^+$) 321.0572; found: 321.0575.

Compound 3q. Yellow crystals; mp 172–173 °C (lit.[5a] 167.2–169.3 °C); yield: 85% (lit.[5a] 61%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56–7.58 (2H, m, Ar*H*), 7.48–7.51 (2H, m, Ar*H*), 7.26–7.29 (2H, m, Ar*H*), 6.94–6.97 (2H, m, Ar*H*), 6.80 (1H, s, Ar*H*), 5.77 (2H, s, NH_2), 3.84 (3H, s, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.3, 149.3, 144.7, 142.4, 137.1, 134.5, 129.8, 129.3, 128.9, 128.6, 128.4, 131.1, 116.4, 114.5, 97.2, 55.4. MS (EI) m/z (%) = 345 (M^+, 38), 114 (100). HRMS (EI) calcd. for $C_{20}H_{15}N_3O_3$ ([M]$^+$) 345.1113; found: 345.1111.

Compound 3r. Yellow crystals; mp 190–191 °C; yield: 83%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49–7.59 (5H, m, Ar*H*), 7.33 (1H, t, *J* 8.0 Hz, Ar*H*), 6.86–6.96 (3H, m, Ar*H*), 6.60 (1H, s, Ar*H*), 5.85 (2H, s, NH_2), 3.81 (3H, s, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 149.4, 144.7, 142.7, 138.5, 137.0, 134.3, 130.0, 129.9, 128.9, 128.4, 121.0, 119.5, 115.7, 114.3, 113.0, 97.7, 55.3. MS (EI) m/z (%) = 346 ($M^+ + 1$, 24), 345 (M^+, 100). HRMS (EI) calcd. for $C_{20}H_{15}N_3O_3$ ([M]$^+$) 345.1113; found: 345.1104.

Compound 3s. Yellow crystals; mp 218–219 °C; yield: 82%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (1H, d, *J* 2.5 Hz, Ar*H*), 8.23 (1H, s, Ar*H*), 7.58–7.63 (4H, m, Ar*H*), 7.53 (3H, t, *J* 3.0 Hz, Ar*H*), 6.78 (1H, s, Ar*H*), 6.21 (2H, s, NH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.1, 144.3, 137.1, 136.8, 134.7, 129.9, 129.0, 128.4, 128.1, 127.4, 121.3, 115.7, 97.8. IR (KBr) ν_{max}: 3464, 3358, 2217, 1536, 1492. MS (EI): m/z (%) = 361 ($M^+ + 1$, 21), 360 (M^+, 100). HRMS (EI) calcd. for $C_{19}H_{12}N_4O_4$ ([M]$^+$) 360.0859; found: 360.0867.

3-Amino-5-cyclohexyl-4-nitrobiphenyl-2-carbonitrile (3t). Yellow crystals; mp 167–168 °C; yield: 84%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–7.55 (5H, m, Ar*H*), 6.80 (1H, s, Ar*H*), 5.48 (2H, s, Ar*H*), 2.76–2.82 (1H, m, C*H*), 1.78–1.93 (m, 5H), 1.22–1.46 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.9, 148.0, 143.9, 137.6, 135.9, 129.5, 128.8, 128.4, 120.1, 117.8, 115.9, 96.1, 68.6, 40.3, 37.2, 33.7, 26.4, 25.8. MS (EI) m/z (%) = 321 (M^+, 7), 304 (100). HRMS (EI) calcd. for $C_{19}H_{19}N_3O_2$ ([M]$^+$) 321.1477; found: 321.1481.

2-(4-Nitro-1,3-diphenylbutylidene)malononitrile (4a). White crystals; mp 101–102 °C; yield: 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.34 (5H, m, Ar*H*), 7.20–7.26 (2H, m, Ar*H*), 6.96–6.99 (2H, m, Ar*H*), 4.52–4.65 (2H, m, CH_2NO_2), 3.36–3.46 (3H, m, CH_2CH), 2.45 (3H, s, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.4, 143.7, 135.5, 130.5, 130.1, 129.3, 128.8, 127.7, 127.5, 112.5, 85.9, 79.1, 42.8, 39.9, 21.6. MS (EI): m/z (%) = 331 (M^+, 2), 104 (100). HRMS (EI) calcd. for $C_{20}H_{17}N_3O_2$ ($[M]^+$) 331.1321; found: 331.1316.

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