Synthesis of Polyfunctionalized 1,4-Dihydropyridine-Fused-1,3-Diazaheterocycles: One-Pot Reaction of 1,1-Bis(methylthio)-2-nitroethylene, 1,*n*-Diamine, Arylaldehyde, and Malononitrile

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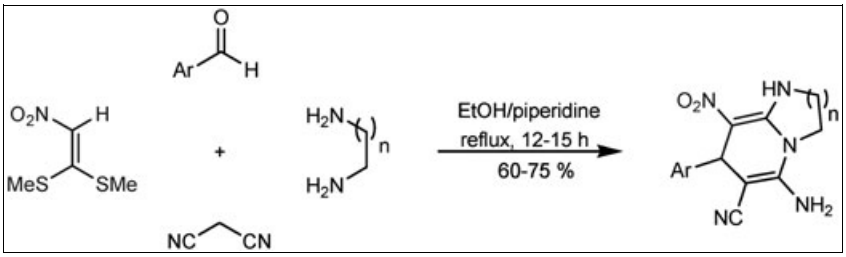

An efficient, one-pot synthetic protocol for polyfunctionalized 1,4-dihydropyridine-fused-1,3-diazaheterocycles, a class of biologically active compounds, starting from 1,1-bis(methylthio)-2-nitroethylene, 1,*n*-diamine, arylaldehyde, and malononitrile is described. The reactions are completed within 12–15 h under refluxing conditions and in the presence of 10 mol % of piperidine as a basic catalyst to produce the title compounds in 60–75% yields.

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INTRODUCTION

Six-membered nitrogen-containing heterocycles, such as pyridines, quinoline, and isoquinoline, are important constituents that often exist in biologically active natural products and synthetic compounds of medicinal interest. Among them, 1,4-dihydropyridines (1,4-DHPs) have received much attention because of their wide range of pharmaceutical and biological properties such as bronchodilator, antiviral, antibacterial, antihypertensive, and anticancer effects [1]. They serve as key intermediates in biogenesis of indol alkaloids [2]. 1,4-Dihydropyridine-containing drugs, such as nifedipine **1**, nicardipine **2**, and others have been found to be useful as calcium channel blockers, and are used most frequently as cardiovascular agents for the treatment of hypertension (Fig. 1) [3]. The classical synthesis of a 1,4-dihydropyridine (1,4-DHP) is a three-component condensation reaction of aldehyde, alkylacetoacetate, and ammonia under acidic condition or in refluxing alcohol that was reported by Hantzsch. This method suffers from disadvantages, such as high temperatures, long reaction times, harsh reaction conditions, and incomplete conversion of reactants [4]. Thus, the development of new and simple synthetic methods for the preparation of 1,4-dihydropyridine derivatives has become an interesting challenge.

Heterocyclic ketene aminals (HKAs) have been significantly used as powerful and versatile synthons for the construction of a wide variety of heterocycles [5]. One of the most conspicuous features of heterocyclic ketene aminals is their bisnucleophilicity *via* the α-carbon and the secondary amino nitrogen toward biselectrophilic reagents and this has been successfully and frequently applied in the preparation of a wide range of fused-ring polycyclic heterocycles. These fused heterocyclic frameworks are frequently found in pharmacophores and play important roles in the drug industry [6–8]. Considering the above reports, the development of new and simple synthetic methods for the efficient preparation of the 1,4-dihydropyridine-fused-1,3-diazaheterocycles will be a beneficial and interesting challenge.

RESULTS AND DISCUSSION

As a part of our ongoing investigations aimed at expanding libraries of the aforementioned bioactive compounds [9] and in continuing of our previous research on the one-pot synthesis of spirooxindole derivatives containing 1,4-dihydropyridine-fused-1,3-diazaheterocycle fragments [10], we described here a four-component reaction of 1,1-bis(methylthio)-2-nitroethylene, 1,*n*-diamine **3**, arylaldehyde **4**, and malononitrile in ethanol as solvent and in the presence of 10 mol% piperidine as a basic catalyst under reflux to afford a series of 1,4-dihydropyridine-fused-1,3-diazaheterocycle derivatives in 60–75% yields (Table 1).

Compounds **5a**–**j** are stable solids and their structures were elucidated from their mass, IR and high field ^{1}H and ^{13}C-NMR spectra as described for **5a**. The IR spectrum of **5a** showed absorption bands due to the NH_2 and

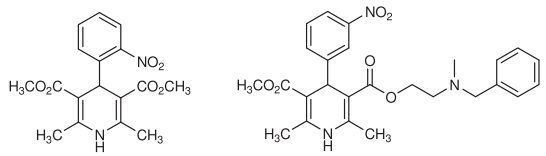
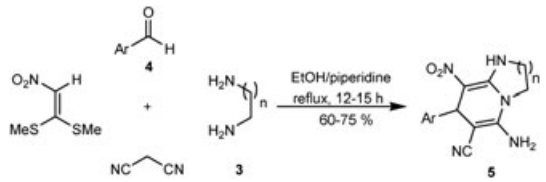


Figure 1. 1,4-Dihydropyridine-containing drugs.

Table 1

The reaction of 1,1-bis(methylthio)-2-nitroethylene, 1,*n*-diamine **3**, arylaldehyde **4**, and malononitrile in EtOH under reflux conditions.

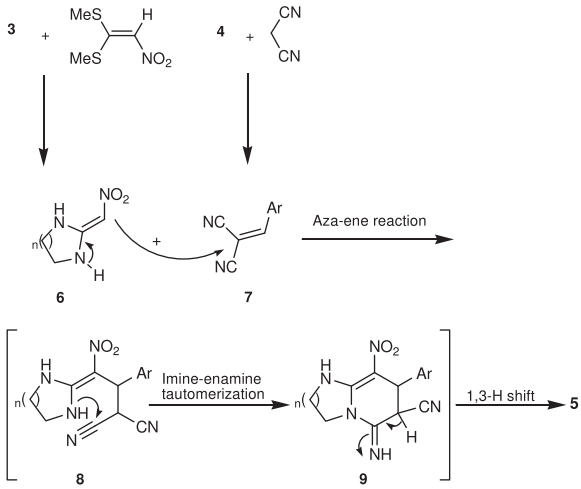


Product	3	Ar	Yield (%)
5a	1,2-Ethanediamine	C_6H_5	75
5b	1,2-Ethanediamine	4-ClC_6H_4	68
5c	1,2-Ethanediamine	4-$O_2NC_6H_4$	70
5d	1,3-Propanediamine	C_6H_5	71
5e	1,3-Propanediamine	4-ClC_6H_4	68
5f	1,4-Butanediamine	C_6H_5	73
5g	1,4-Butanediamine	4-$O_2NC_6H_4$	60
5h	2,2-Dimethyl-1,3-propanediamine	C_6H_5	70
5i	2,2-Dimethyl-1,3-propanediamine	4-ClC_6H_4	65
5j	2,2-Dimethyl-1,3-propanediamine	4-$O_2NC_6H_4$	68

NH groups at 3446, 3352, and 3219 cm^{-1}. Stretching frequencies related to CN, and C=C functional groups appeared at 2186, and 1650 cm^{-1}, respectively. Three sharp singlet signals recognized as arising from a CH group (δ = 4.59), NH_2 group (δ = 6.47), and NH group (δ = 9.48) appeared in the ^{1}H-NMR spectrum of **5a**. The phenyl moiety gave rise to characteristic signals in the aromatic region of the spectrum. ^{1}H-decoupled ^{13}C-NMR spectrum of **5a** showed 12 distinct signals in agreement with the proposed structures. Resonances due to *C*-CN, *C*-NO_2, *C*N, and C_{ipso}-CH, appearing at δ = 59.27, 105.67, 120.86, and 144.95 ppm, respectively. However, no molecular ion peak was exhibited in the mass spectrum of **5a** but two fragmentations that related to C_6H_5 and $C_8H_9N_5O_2$ molecular formulas appeared at *m/z* 77 and 206.

A plausible reaction mechanism is suggested in the Scheme 1. At first, the reaction of 1,1-bis(methylthio)-2-nitroethylene and 1,*n*-diamine **3** produces heterocyclic ketene aminal **6** that is effective aza-ene component. In the next step the addition of arylaldehyde **4**, malononitrile, and piperidine as a basic catalyst to the reaction pot lead to the formation of arylidenemalononitrile **7**, which *in situ* is formed from Knoevenagel condensation of malononitrile and arylaldehyde **4**. The aza-ene reaction between heterocyclic ketene aminal **6** and arylidenemalononitrile **7** gives the intermediate **8**, which undergoes successive imine-enamine tautomerization, followed by nucleophilic addition of the secondary amino group to the cyano group, resulting in the formation of intermediate **9**. Finally 1,3-H migration or imine-enamine tautomerization gives the title compound **5**.

Scheme 1. Plausible mechanism for the formation of compound **5**.



CONCLUSION

In summary, we have reported a one-pot method for the construction of 1,4-dihydropyridine-fused-1,3-diazaheterocycle derivatives from simple and commercially available starting material under mild condition. The advantages of the present procedure are simplicity of the operation. In addition, workup and purification of products are simple. Furthermore, the number of functional groups that exist in these types of heterocycles lead to the biological activities of the title compounds.

EXPERIMENTAL

All chemicals were purchased from Merck or Aldrich and were used without further purification. Melting points measured on an Electrothermal 9100 apparatus. IR spectra were recorded as KBr pellets on FT-IR spectrometer. ^{1}H-NMR (500.13 MHz) and ^{13}C-NMR (125.75 MHz) spectra were obtained using a Bruker DRX-500 AVANCE spectrometer. All NMR spectra were determined in DMSO-d_6. Chemical shifts are reported in parts per

million (δ) downfield from an internal tetramethylsilane reference. Coupling constants (*J* values) are reported in hertz (Hz), and spin multiplicities are indicated by the following symbols: s (singlet), d (doublet), t (triplet), m (multiplet). Mass spectra were recorded on a FINNIGAN-MATT 8430 mass spectrometer operating at an ionization potential of 20 or 70 eV.

General procedure for the synthesis of 5-amino-8-nitro-7-phenyl-1,2,3,7-tetrahydroimidazo[1,2-*a*]pyridine-6-carbonitrile (5a). To a magnetically stirred solution of 1,1-bis(methylthio)-2-nitroethylene (0.16 g, 1 mmol) in EtOH (3 mL), 1,2-ethanediamine (0.06 g, 1 mmol) was added. The reaction mixture was then stirred for 7 h. After that, benzaldehyde (0.10 g, 1 mmol), malononitrile (0.06 g, 1 mmol), and piperidine (10 mol %) were added simultaneously. The reaction mixture was stirred for 7 h under refluxing condition and the progress of the reaction was followed by thin layer chromatography. After completion, the reaction mixture was filtered and the precipitate was washed with cool EtOH (4 mL) and CH_2Cl_2 (5 mL) to afford the pure product **5a** (0.21 g, 75%), as yellow powder; mp = 180°C. IR (KBr): 3446, 3352, and 3219 (NH_2 and NH), 2186 (CN), 1650 (C═C), 1468 (CH_2), 1360 (NO_2) cm^{-1}. ^{1}H-NMR (500.13 MHz, DMSO-d_6): δ_H = 3.78–3.82 (2 H, m, CH_2NH), 3.94–4.04 (2 H, m, CH_2N), 4.59 (1 H, s, CH), 6.47 (2 H, s, NH_2), 7.15–7.18 (3 H, m, Ph), 7.24–7.27 (2 H, m, Ph), 9.48 (1 H, s, NH). ^{13}C-NMR (125.75 MHz, DMSO-d_6): δ_C = 40.78 (CH), 43.23 (CH_2), 44.62 (CH_2), 59.27 (*C*-CN), 105.67 (C-NO_2), 120.86 (CN), 126.37 (CH_{para} of Ph), 126.89 (2 CH_{meta} of Ph), 128.06 (2 CH_{ortho} of Ph), 144.95 (C_{ipso}-CH), 149.31 (NH_2*C*N), 151.60 (N*C*NH). MS: *m/z* (%) = 275 (2), 261 (3), 248 (32), 234 (100), 219 (23), 206 (15), 175 (6), 158 (4), 114 (9), 103 (4), 77 (9). Anal. Calcd for $C_{14}H_{13}N_5O_2$ (283.29): C, 59.36; H, 4.63; N, 24.72. Found: C, 59.47; H, 4.65; N, 24.33.

5-Amino-7-(4-chlorophenyl)-8-nitro-1,2,3,7-tetrahydroimidazo[1,2-*a*]pyridine-6-carbonitrile (5b). Yield: 0.21 g (68%); yellow crystals; mp = 270°C (dec). IR (KBr): 3400, 3342, and 3218 (NH_2 and NH), 2176 (CN), 1660 (C═C), 1467 (CH_2), 1372 (NO_2) cm^{-1}. ^{1}H-NMR (500.13 MHz, DMSO-d_6): δ_H = 3.80–3.83 (2 H, m, CH_2NH), 3.99–4.00 (2 H, m, CH_2N), 4.61 (1 H, s, CH), 6.51 (2 H, s, NH_2), 7.20 (2 H, d, $^3J_{H,H}$ = 7.6 Hz, 2 CH of Ar), 7.31 (2 H, d, $^3J_{H,H}$ = 7.6 Hz, 2 CH of Ar), 9.39 (1 H, s, NH). ^{13}C NMR (125.75 MHz, DMSO-d_6): δ_C = 40.36 (CH), 43.26 (CH_2), 44.63 (CH_2), 58.67 (*C*-CN), 105.37 (C-NO_2), 120.77 (CN), 128.00 (2 CH of Ar), 128.87 (2 CH of Ar), 130.87 (C_{ipso}-Cl), 143.96 (C_{ipso}-CH), 149.35 (N*C*NH), 151.47 (NH_2*C*N). MS: *m/z* (%) = 296 (8), 282 (8), 248 (12), 234 (12), 219 (7), 194 (4), 149 (10), 137 (10), 123 (14), 109 (15), 97 (38), 81 (45), 69 (100), 57 (70). Anal. Calcd for $C_{14}H_{12}ClN_5O_2$ (317.73): C, 52.92; H, 3.81; N, 22.04. Found: C, 52.85; H, 3.72; N, 22.10.

5-Amino-8-nitro-7-(4-nitrophenyl)-1,2,3,7-tetrahydroimidazo[1,2-*a*]pyridine-6-carbonitrile (5c). Yield: 0.23 g (70%); yellow crystals; mp = 244°C (dec). IR (KBr): 3425, 3336, and 3237 (NH_2 and NH), 2182 (CN), 1661 (C═C), 1513 and 1349 (NO_2), 1465 (CH_2) cm^{-1}. ^{1}H-NMR (500.13 MHz, DMSO-d_6): δ_H = 3.77–3.86 (2 H, m, CH_2NH), 3.95–4.05 (2 H, m, CH_2N), 4.76 (1 H, s, CH), 6.64 (2 H, s, NH_2), 7.46 (2 H, d, $^3J_{H,H}$ = 8.4 Hz, 2 CH of Ar), 8.14 (2 H, d, $^3J_{H,H}$ = 8.4 Hz, 2 CH of Ar), 9.59 (1 H, s, NH). ^{13}C-NMR (125.75 MHz, DMSO-d_6): δ_C = 40.95 (CH), 43.39 (CH_2), 44.69 (CH_2), 57.81 (*C*-CN), 104.87 (C-NO_2), 120.56 (CN), 123.48 (2 CH of Ar), 128.26 (2 CH of Ar), 146.18 (C_{ipso}-NO_2), 149.65 (N*C*NH), 151.52 (NH_2*C*N), 152.64 (C_{ipso}-CH). MS: *m/z* (%) = 328 (M^+, 5), 326 (100), 310 (21), 296 (31), 281 (48), 263 (7), 248 (26), 234 (67), 221 (10), 206 (43), 179 (16), 165 (18), 152 (22), 140 (14), 127 (14), 69 (21), 57 (14). Anal. Calcd for $C_{14}H_{12}N_6O_4$ (328.28): C, 51.22; H, 3.68; N, 25.60. Found: C, 51.34; H, 3.70; N, 25.55.

6-Amino-9-nitro-8-phenyl-1,3,4,8-tetrahydro-2*H*-pyrido[1,2-*a*]pyrimidine-7-carbonitrile (5d). Yield: 0.21 g (71%); yellow crystals; mp = 247 °C (dec). IR (KBr): 3337 and 3229 (NH_2 and NH), 2181 (CN), 1647 (C═C), 1454 and 1425 (CH_2), 1337 (NO_2) cm^{-1}. ^{1}H-NMR (500.13 MHz, DMSO-d_6): δ_H = 1.83–1.95 (1 H, m, $NCH_2CH_2CH_2NH$), 2.10–2.34 (1 H, m, $NCH_2CH_2CH_2NH$), 3.32–3.36 (1 H, m, $NCH_2CH_2CH_2NH$), 3.45–3.59 (1 H, m, $NCH_2CH_2CH_2NH$), 3.73–3.80 (2 H, m, $NCH_2CH_2CH_2NH$), 4.66 (1 H, s, CH), 6.39 (2 H, s, NH_2), 7.13 (2 H, d, $^3J_{H,H}$ = 7.5 Hz, Ph), 7.18 (1 H, t, $^3J_{H,H}$ = 7.2 Hz, Ph), 7.26 (2 H, t, $^3J_{H,H}$ = 7.5 Hz, Ph), 11.50 (1 H, s, NH). ^{13}C-NMR (125.75 MHz, DMSO-d_6): δ_C = 19.66 (CH), 38.37 ($NCH_2CH_2CH_2NH$), 40.09 ($NCH_2CH_2CH_2NH$), 43.02 ($NCH_2CH_2CH_2NH$), 61.19 (*C*-CN), 107.88 (C-NO_2), 120.72 (CN), 124.20 (CH_{para} of Ph), 126.51 (2 CH_{meta} of Ph), 128.29 (2 CH_{ortho} of Ph), 144.19 (C_{ipso}-CH), 150.40 (NH_2*C*N), 150.81 (N*C*NH). MS: *m/z* (%) = 297 (M^+, 13), 279 (6), 264 (8), 251 (100), 236 (7), 220 (37), 207 (5), 194 (18), 174 (10), 164 (4), 154 (8), 140 (21), 128 (17), 118 (9), 93 (24), 77 (27), 69 (14), 57 (16). Anal. Calcd for $C_{15}H_{15}N_5O_2$ (297.31): C, 60.60; H, 5.09; N, 23.56. Found: C, 60.75; H, 5.12; N, 23.60.

6-Amino-8-(4-chlorophenyl)-9-nitro-1,3,4,8-tetrahydro-2*H*-pyrido[1,2-*a*]pyrimidine-7-carbonitrile (5e). Yield: 0.21 g (68%); yellow crystals; mp = 267°C (dec). IR (KBr): 3386, 3344, and 3227 (NH_2 and NH), 2187 (CN), 1661 and 1630 (C═C), 1488 and 1428 (CH_2), 1350 (NO_2) cm^{-1}. ^{1}H-NMR (500.13 MHz, DMSO-d_6): δ_H = 2.10–2.49 (2 H, m, $NCH_2CH_2CH_2NH$), 3.30–3.35 (2 H, m, $NCH_2CH_2CH_2NH$), 3.73–3.78 (2 H, m, $NCH_2CH_2CH_2NH$), 4.68 (1 H, s, CH), 6.41 (2 H, s, NH_2), 7.17 (2 H, d, $^3J_{H,H}$ = 6.7 Hz, Ar), 7.31 (2 H, d, $^3J_{H,H}$ = 6.7 Hz, Ar), 11.50 (1 H, s, NH). ^{13}C-NMR (125.75 MHz, DMSO-d_6): δ_C = 19.57 (CH), 38.37 ($NCH_2CH_2CH_2NH$), 38.84 ($NCH_2CH_2CH_2NH$), 43.04 ($NCH_2CH_2CH_2NH$), 60.67 (*C*-CN), 107.63 (C-NO_2), 120.55 (CN), 128.21 (2 CH of Ar), 128.48 (2 CH of Ar), 131.06 (C_{ipso}-Cl), 143.14 (C_{ipso}-CH), 150.30 (N*C*NH), 150.92 (NH_2*C*N). MS: *m/z* (%) = 299 (5), 279 (3), 267 (5), 248 (14), 220 (10), 176 (6), 167 (9), 149 (18), 125 (25), 111 (27), 97 (43), 83 (45), 69 (69), 57 (100). Anal. Calcd for $C_{15}H_{14}ClN_5O_2$ (331.76): C, 54.31; H, 4.25; N, 21.11. Found: C, 54.35; H, 4.33; N, 21.15.

7-Amino-10-nitro-9-phenyl-1,2,3,4,5,9-hexahydropyrido[1,2-*a*][1,3]diazepine-8-carbonitrile (5f). Yield: 0.23 g (73%); yellow crystals; mp = 275°C (dec). IR (KBr): 3455 and 3364 (NH_2 and NH), 2183 (CN), 1650 and 1603 (C═C), 1450 and 1418 (CH_2), 1352 (NO_2) cm^{-1}. ^{1}H-NMR (500.13 MHz, DMSO-d_6): δ_H = 1.48–1.50 (1 H, m, CH_2), 1.77–1.79 (2 H, m, CH_2), 1.94–2.00 (1 H, m, CH_2), 3.25–3.26 (2 H, m, CH_2), 3.76–3.80 (1 H, m, CH_2), 4.01–4.08 (1 H, m, CH_2), 4.77 (1 H, s, CH), 6.37 (2 H, s, NH_2), 7.11 (2 H, d, $^3J_{H,H}$ = 7.4 Hz, 2 CH of Ph), 7.21 (1 H, t, $^3J_{H,H}$ = 7.2 Hz, CH of Ph), 7.29 (2 H, t, $^3J_{H,H}$ = 7.4 Hz, 2 CH of Ph), 10.52 (1 H, s, NH). ^{13}C-NMR (125.75 MHz, DMSO-d_6): δ_C = 25.08 (2 CH_2), 26.35 (CH), 45.06 (CH_2NH), 52.77 (CH_2N), 64.69 (*C*-CN), 112.77 (C-NO_2), 120.28 (CN), 126.20 (2 CH_{meta} of Ph), 126.73 (CH_{para} of Ph), 128.60 (2 CH_{ortho} of Ph), 143.43 (C_{ipso}-CH), 154.26 (NH_2*C*N), 157.03 (N*C*NH). MS: *m/z* (%) = 313 (M^++2, 7), 311 (M^+, 5), 293 (6), 279 (5), 265 (53), 248 (23), 234 (22), 219 (17), 206 (9), 194 (8), 170 (7), 157 (53), 140 (14), 127 (20), 111 (21), 97 (37), 83 (44), 69 (59), 55 (100). Anal. Calcd for $C_{16}H_{17}N_5O_2$ (311.34): C, 61.73; H, 5.50; N, 22.49. Found: C, 61.78; H, 5.62; N, 22.52.

7-Amino-10-nitro-9-(4-nitrophenyl)-1,2,3,4,5,9-hexahydropyrido[1,2-*a*][1,3]diazepine-8-carbonitrile (5g). Yield: 0.21 g (60%); yellow crystals; mp = 235°C (dec). IR (KBr): 3388, 3330, and 3217 (NH_2 and NH), 2191 (CN), 1653 and 1624 (C═C), 1525 and 1335 (NO_2), 1425 (CH_2) cm^{-1}. ^{1}H-NMR (500.13 MHz, DMSO-d_6): δ_H = 1.50–1.53 (1 H, m, CH_2), 1.79–1.81 (2 H, m, CH_2), 1.98–2.00 (1 H, m, CH_2), 3.35–3.39 (2 H, m, CH_2), 3.75–3.78 (1 H, m, CH_2), 4.04–4.06 (1 H, m, CH_2), 4.93 (1 H, s, CH), 6.49 (2 H, s, NH_2), 7.40 (2 H, d, $^3J_{H,H}$ = 7.6 Hz, 2 CH of Ar), 8.16 (2 H, d, $^3J_{H,H}$ = 7.6 Hz, 2 CH of Ar), 10.56 (1 H, s, NH). ^{13}C-NMR (125.75 MHz, DMSO-d_6): δ_C = 24.94 (2 CH_2), 26.24 (CH), 45.10 (CH_2NH), 52.78 (CH_2N), 62.81 (*C*-CN), 111.80 (C-NO_2), 119.97 (CN), 123.99 (2 CH of Ar), 127.52 (2 CH of Ar), 146.37 (C_{ipso}-NO_2), 150.99 (N*C*NH), 154.68 (NH_2*C*N), 157.00 (C_{ipso}-CH). MS: *m/z* (%) = 340 (7), 310 (5), 285 (6), 265 (10), 248 (15), 219 (17), 199 (27), 169 (13), 146 (30), 126 (25), 104 (18), 84 (100), 57 (80). Anal. Calcd for $C_{16}H_{16}N_6O_4$ (356.34): C, 53.93; H, 4.53; N, 23.58. Found: C, 53.97; H, 4.58; N, 23.66.

6-Amino-3,3-dimethyl-9-nitro-8-phenyl-1,3,4,8-tetrahydro-2*H*-pyrido[1,2-*a*]pyrimidine-7-carbonitrile (5h). Yield: 0.23 g (70%); yellow crystals; mp = 277°C (dec). IR (KBr): 3382, 3340, and 3227 (NH_2 and NH), 2187 (CN), 1661 and 1627 (C═C), 1502 and 1340 (NO_2), 1422 (CH_2) cm^{-1}. ^{1}H-NMR (500.13 MHz, DMSO-d_6): δ_H = 0.98 (3 H, s, Me), 1.06 (3 H, s, Me), 3.24 (2 H, AB system, $^2J_{H,H}$ = 13.2 Hz, C*H*$_2$NH), 3.49 (2 H, AB system, $^2J_{H,H}$ = 13.0 Hz, C*H*$_2$N), 4.70 (1 H, s, CH), 6.41 (2 H, s, NH_2), 7.12 (2 H, d, $^3J_{H,H}$ = 7.1 Hz, 2 CH of Ph), 7.18 (1 H, t, $^3J_{H,H}$ = 7.3 Hz, CH of Ph), 7.27 (2 H, t, $^3J_{H,H}$ = 7.4 Hz, 2 CH of Ph), 11.47 (1 H, s, NH). ^{13}C-NMR (125.75 MHz, DMSO-d_6): δ_C = 22.38 (CH_3), 23.78 (CH_3), 27.02 (CH), 38.68 (C^3), 49.12 (CH_2N), 53.11 (CH_2NH), 61.13 (*C*-CN), 107.67 (C-NO_2), 120.67 (CN), 126.35 (2 CH_{ortho} of Ph), 126.60 (CH_{para} of Ph), 128.32 (2 CH_{meta} of Ph), 144.10 (C_{ipso}-CH), 149.52 (N*C*NH), 150.94 (NH_2*C*N). MS: *m/z* (%) =326 (M^++1, 85), 325 (M^+, 10), 310 (23), 294 (55), 279 (90), 263 (14), 248 (100), 234 (78), 219 (55), 206 (98), 194 (17), 178 (18), 164 (28), 151 (32), 139 (22), 127 (23), 114 (22), 69 (55), 55 (50). Anal. Calcd for $C_{17}H_{19}N_5O_2$ (325.37): C, 62.76; H, 5.89; N, 21.52. Found: C, 62.85; H, 5.90; N, 21.60.

6-Amino-8-(4-chlorophenyl)-3,3-dimethyl-9-nitro-1,3,4,8-tetrahydro-2*H*-pyrido[1,2-*a*]pyrimidine-7-carbonitrile (5i). Yield: 0.23 g (65%); yellow crystals; mp = 270°C (dec). IR (KBr): 3345 and 3230 (NH_2 and NH), 2187 (CN), 1663 (C═C), 1440 (CH_2), 1348 (NO_2) cm^{-1}. ^{1}H-NMR (500.13 MHz, DMSO-d_6): δ_H = 0.97 (3 H, s, Me), 1.05 (3 H, s, Me), 3.23 (2 H, AB system, $^2J_{H,H}$ = 13.1 Hz, C*H*$_2$NH), 3.49 (2 H, AB system, $^2J_{H,H}$ = 11.9 Hz, C*H*$_2$N), 4.71 (1 H, s, CH), 6.47 (2 H, s, NH_2), 7.14 (2 H, d, $^3J_{H,H}$ = 7.6 Hz, 2 CH of Ar), 7.34 (2 H, d, $^3J_{H,H}$ = 7.6 Hz, 2 CH of Ar), 11.46 (1 H, s, NH). ^{13}C-NMR (125.75 MHz, DMSO-d_6): δ_C = 22.46 (CH_3), 23.72 (CH_3), 26.98 (CH), 38.67 (C^3), 49.15 (CH_2N), 53.07 (CH_2NH), 60.53 (*C*-CN), 107.40 (C- NO_2), 120.52 (CN), 128.27 (2 CH of Ar), 128.29 (2 CH of Ar), 131.14 (C_{ipso}-Cl), 143.04 (N*C*NH), 149.41 (NH_2*C*N), 151.06 (C_{ipso}-CH). MS: *m/z* (%) = 313 (3), 248 (7), 236 (9), 219 (7), 206 (3), 147 (10), 129 (12), 111 (20), 85 (25), 83 (100), 57 (53). Anal. Calcd for $C_{17}H_{18}ClN_5O_2$ (359.81): C, 56.75; H, 5.04; N, 19.46. Found: C, 56.80; H, 5.00; N, 19.50.

6-Amino-3,3-dimethyl-9-nitro-8-(4-nitrophenyl)-1,3,4,8-tetrahydro-2*H*-pyrido[1,2-*a*]pyrimidine-7-carbonitrile (5j). Yield: 0.25 g (68%); yellow crystals; mp = 236°C (dec). IR (KBr): 3342 and 3223 (NH_2 and NH), 2186 (CN), 1658 and 1625 (C═C), 1517 and 1348 (NO_2), 1426 (CH_2) cm^{-1}. ^{1}H-NMR (500.13 MHz, DMSO-d_6): δ_H = 0.99 (3 H, s, Me), 1.05 (3 H, s, Me), 3.25 (2 H, AB system, $^2J_{H,H}$ = 12.3 Hz, C*H*$_2$NH), 3.51 (2 H, AB system, $^2J_{H,H}$ = 11.0 Hz, C*H*$_2$N), 4.85 (1 H, s, CH), 6.57 (2 H, s, NH_2), 7.39 (2 H, d, $^3J_{H,H}$ = 5.9 Hz, 2 CH of Ar), 8.16 (2 H, d, $^3J_{H,H}$ = 5.9 Hz, 2 CH of Ar), 11.47 (1 H, s, NH). ^{13}C-NMR (125.75 MHz, DMSO-d_6): δ_C = 22.59 (CH_3), 23.68 (CH_3), 26.97 (CH), 38.20 (C^3), 49.17 (CH_2N), 53.07 (CH_2NH), 59.58 (*C*-CN), 106.84 (C-NO_2), 120.32 (CN), 123.75 (2 CH of Ar), 127.64 (2 CH of Ar), 146.28 (C_{ipso}-NO_2), 149.39 (N*C*NH), 151.29 (NH_2*C*N), 151.70 (C_{ipso}-CH). MS: *m/z* (%) = 368 (6), 321 (4), 278 (7), 264 (5), 247 (55), 236 (12), 219 (37), 206 (3), 194 (4), 175 (8), 148 (14), 139 (8), 128 (21), 111 (21), 97 (42), 83 (51), 69 (78), 55 (100). Anal. Calcd for $C_{17}H_{18}N_6O_4$ (370.36): C, 55.13; H, 4.90; N, 22.69. Found: C, 55.18; H, 4.92; N, 22.72.

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