The First Synthesis of Allyl Isonitriles from Baylis–Hillman Adducts, and Their Application in the Synthesis of Substituted Imidazo[1,2-*a*]pyridines and Tetraazadibenzoazulenes[1]

Maloy Nayak,[a] Sanjeev Kanojiya,[b] Sanjay Batra*[a]

[a] Medicinal and Process Chemistry Division, Central Drug Research Institute, PO Box 173, Lucknow 226 001, India

[b] SAIF Division, Central Drug Research Institute, PO Box 173, Lucknow 226 001, India
Fax +91(522)2623405, +91(522)2623938; E-mail: batra_san@yahoo.co.uk

Received 11 August 2008

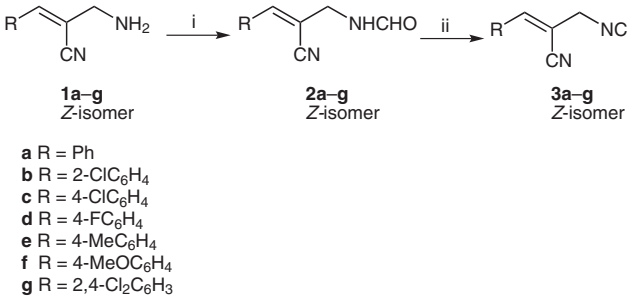
Abstract: The first report of the stereoselective synthesis of substituted allyl isonitriles from primary allylamines generated from Baylis–Hillman adducts, and their utilization in a robust isonitrile-based multicomponent reaction in the presence of ammonium chloride to afford substituted imidazo[1,2-*a*]pyridines, is described.

Key words: isonitriles, Baylis–Hillman, allylamines, multicomponent reactions, imidazo[1,2-*a*]pyridines

The development of novel synthetic intermediates which lead to the formation of multiple-ring-containing heterocyclic systems is a progressive feature of synthetic organic chemistry. The Baylis–Hillman reaction is considered to be a complexity generating, C–C bond-forming reaction. Perhaps the three chemospecific functional groups present in the products of this reaction makes them an attractive option for achieving the synthesis of an array of diverse molecular frameworks.[2] Not only these products, but also the derivatives furnished from them, have been innovatively employed in the development of facile and general approaches for the generation of novel compounds, including the aforementioned heterocycles. One such useful intermediate, which can be readily and stereoselectively synthesized from Baylis–Hillman adducts, are substituted primary allylamines.[3] Such allylamines have been demonstrated by us to be viable precursors for several nitrogen-containing heterocyclic systems.[4] In our recent report[2] we have proposed that the *N*-formyl derivatives, which can be readily synthesized by the reaction of the primary allylamines with formamide,[4b] may be utilized for the synthesis of substituted isonitriles, which in turn may serve as one of the reactants in several of the well-established isonitrile-based multicomponent reactions (IMCRs).[5] We have now been able to optimize the preparation of these substituted isonitriles and have used them as one of the reactants in an IMCR to afford substituted imidazo[1,2-*a*]pyridines. Further, the substituted imidazopyridines have been used as substrates for obtaining the novel tetraazadibenzoazulene system. The details of this work are presented in this communication.

SYNTHESIS 2009, No. 3, pp 0431–0437
Advanced online publication: 09.01.2009
DOI: 10.1055/s-0028-1083306; Art ID: P08408SS

The allylamines **1a–g** were stereoselectively prepared following the reported strategy.[3] Reaction of compounds **1a–g** with formamide at 120 °C for two hours resulted in the required formamides **2a–g**. Treatment of **2a–g** with phosphorus oxychloride in the presence of triethylamine at low temperature gave the desired isonitriles **3a–g** in 46–70% yield (Scheme 1). The stereochemistry of the allyl isonitriles was maintained as *Z*. Strikingly, the molecular ion peak in the mass spectra of the isonitriles, except for **3g** which was a trimer, was observed to correspond to the tetramer (Figure 1). These isonitriles are odorless and are stable at room temperature.



Scheme 1 *Reagents and conditions*: i) $HCONH_2$, 120 °C, 2 h; ii) $POCl_3$, Et_3N, THF, –20 °C to 0 °C, 2 h.

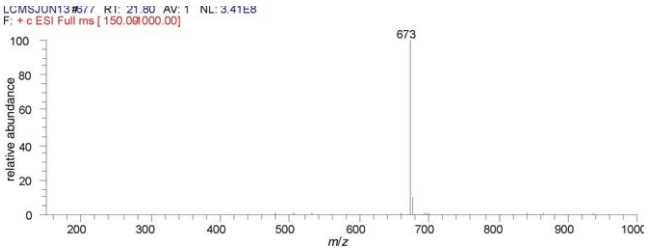
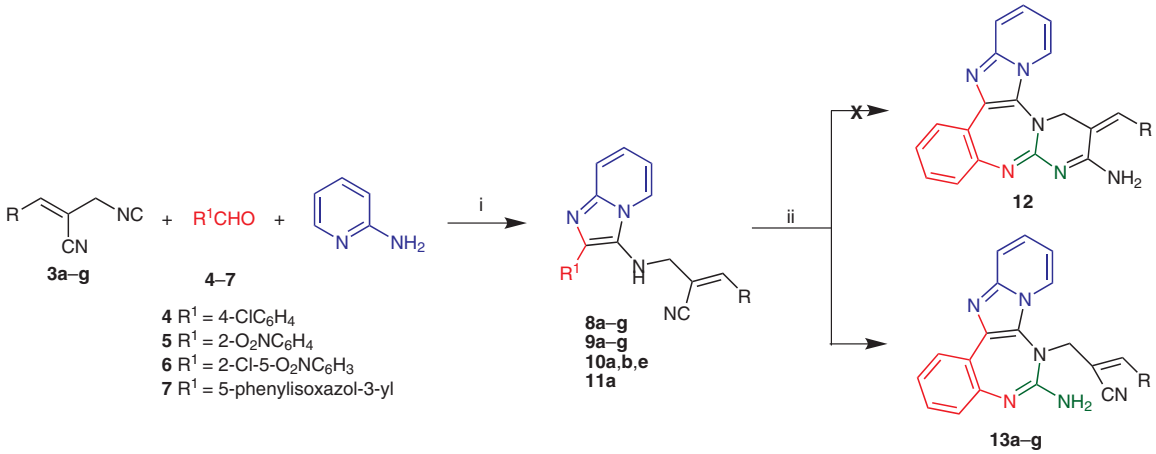


Figure 1 The mass spectrum (ES) of **3a**

One of the most common IMCRs involves the reaction between an isonitrile, 2-aminopyridine and an aldehyde to afford the substituted imidazo[1,2-*a*]pyridine core.[6] Compounds consisting of this scaffold have been ascribed with a variety of pharmacological properties.[7] These include anticancer, anticoccidial, antigastric, antiviral, antithrombotic and antiprotozoal properties. In order to demonstrate the synthetic potential of the isonitriles synthesized during the present study, the reactions of **3a–g** with 2-aminopyri-



Scheme 2 *Reagents and conditions*: i) NH_4Cl, toluene, 110 °C, 5–6 h; ii) a) In–HCl, THF–H_2O (1:1), r.t., 1 h; b) BrCN, K_2CO_3, THF, r.t., 9 h.

dine and different aryl aldehydes **4**–**7** were performed, in the presence of ammonium chloride,[6b] as shown in Scheme 2. It was pleasing to note that all of the isonitriles participated in the multicomponent reaction to yield the substituted imidazo[1,2-*a*]pyridines **8a**–**g**, **9a**–**g**, **10a**,**b**,**e** and **11a** in moderate to good yields.

We have been interested in the synthesis of heterocyclic scaffolds which incorporate the guanidine subunit in the cyclic framework.[2,4c] Consequently, it was envisaged that reduction of the nitro group in 2-(2-nitrophenyl)imidazo[1,2-*a*]pyridines **9** followed by reaction with cyanogen bromide may trigger concomitant intramolecular cyclizations to yield **12** (Scheme 2). Accordingly, as part of the optimization, compound **9a** was treated with In–HCl under aqueous conditions. The reaction was complete within one hour, but purification of the amine by column chromatography was unsuccessful. Therefore, the crude amine was treated with cyanogen bromide in the presence of potassium carbonate in tetrahydrofuran at room temperature; the reaction was complete in nine hours. Workup of the reaction mixture led to the product, which was purified by silica gel column chromatography to obtain pure compound in 62% yield. The spectroscopic analysis, however, established the structure of the product as **13a** instead of the expected **12** (R = Ph). As in the case of **9a**, all other substrates **9b**–**g** were initially reduced in the presence of In–HCl and then reacted with cyanogen bromide to provide **13b**–**g** in 65–73% yield. In the next stage we attempted the intramolecular cyclization between the free amino and the nitrile group in the presence of different bases, but we were unsuccessful.

In summary, we have disclosed the first successful stereoselective synthesis of allyl isonitriles from Baylis–Hillman adducts and have demonstrated their participation in an IMCR to afford substituted imidazo[1,2-*a*]pyridines. These imidazo[1,2-*a*]pyridines were further utilized for the synthesis of the tetraazadibenzoazulene system. Further work to explore the synthetic utility of the substituted isonitriles synthesized herein is under way in our laboratory.

Melting points were determined in capillary tubes on an apparatus containing silicon oil and are uncorrected. IR spectra were recorded using a Perkin Elmer Spectrum RXI FTIR spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on either a Bruker DPX-200 FT or a Bruker Avance DRX-300 spectrometer, using TMS as an internal standard (chemical shifts δ in ppm). ESMS data were recorded on a Micromass Quattro-II LCMS system. HRMS data were recorded as EI-HRMS on a JEOL system. Elemental analyses were performed on a Carlo Erba 108 or an Elementar Vario EL III microanalyzer. Due to the poor solubility of compounds **13a**–**g** even in DMSO-d_6, the ^{13}C NMR spectra could not be recorded.

(*Z*)-2-(Isocyanomethyl)-3-phenylprop-2-enenitrile (3a); Typical Procedure for the Synthesis of Isonitriles 3a–g

Et_3N (7.9 mL, 56.6 mmol) was added to a stirred soln of formamide **2a** (0.5 g, 2.7 mmol) in THF (8.0 mL) and the mixture was cooled to –10 °C in an ice–salt bath. Then, a soln of $POCl_3$ (1.07 mL, 11.35 mmol) in THF (5.0 mL) was added dropwise to the reaction mixture at the same temperature. The mixture was allowed to reach 0 °C and the reaction was continued for another 2 h. Thereafter, the mixture was cooled to –20 °C and the reaction was quenched by the dropwise addition of H_2O (20 mL), which was followed by the further addition of H_2O (100 mL) and extraction with Et_2O (50 mL). The aqueous phase was extracted with Et_2O (2 × 40 mL), and the organic layers were combined, dried (anhyd Na_2SO_4) and concentrated under reduced pressure to afford the crude product. Purification by column chromatography on silica gel (EtOAc–hexanes, 1:3) led to pure **3a** as a yellow oil; yield: 0.3 g (65%); R_f = 0.42 (hexanes–EtOAc, 8:2).

IR (neat): 2150 (NC), 2218 (CN) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.37 (s, 2 H, CH_2), 7.30 (s, 1 H, =CH), 7.41–7.49 (m, 3 H, ArH), 7.78–7.81 (m, 2 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 45.1, 102.5, 116.2, 129.1, 129.2, 129.3, 131.6, 146.2, 161.5.

MS (ES+): *m*/*z* = 673 [4M + 1]$^+$.

(*Z*)-3-(2-Chlorophenyl)-2-(isocyanomethyl)prop-2-enenitrile (3b)

Yield: 60%; yellow solid; mp 72–73 °C; R_f = 0.54 (hexanes–EtOAc, 8:2).

IR (KBr): 2152 (NC), 2219 (CN) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.41 (s, 2 H, CH_2), 7.38–7.43 (m, 2 H, ArH), 7.47–7.50 (m, 1 H, ArH), 7.70 (s, 1 H, =CH), 7.98 (dd, *J* = 2.3, 6.6 Hz, 1 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 45.0, 106.1, 115.6, 127.6, 129.4, 130.3, 130.6, 132.5, 134.8, 143.0, 162.2.

MS (ES–): *m*/*z* = 807 [4M – 1]$^-$, 201 [M – 1]$^-$.

(*Z*)-3-(4-Chlorophenyl)-2-(isocyanomethyl)prop-2-enenitrile (3c)

Yield: 65%; yellow solid; mp 75–76 °C; R_f = 0.28 (hexanes–EtOAc, 8:2).

IR (KBr): 2152 (NC), 2220 (CN) cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 4.38 (s, 2 H, CH_2), 7.26 (s, merged with $CDCl_3$, 1 H, =CH), 7.45 (d, *J* = 8.6 Hz, 2 H, ArH), 7.75 (d, *J* = 8.5 Hz, 2 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 45.0, 103.0, 116.0, 129.6, 130.5, 137.7, 144.6, 162.0.

MS (ES–): *m*/*z* = 807 [4M – 1]$^-$, 201 [M – 1]$^-$.

(*Z*)-3-(4-Fluorophenyl)-2-(isocyanomethyl)prop-2-enenitrile (3d)

Yield: 70%; yellow solid; mp 79–80 °C; R_f = 0.42 (hexanes–EtOAc, 8:2).

IR (KBr): 2152 (NC), 2220 (CN) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.37 (s, 2 H, CH_2), 7.17 (t, *J* = 8.6 Hz, 2 H, ArH), 7.26 (s, merged with $CDCl_3$, 1 H, =CH), 7.81 (d, *J* = 5.3 Hz, 1 H, ArH), 7.83 (d, *J* = 5.3 Hz, 1 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 45.1, 102.2, 116.5, 116.7, 128.4, 131.6, 131.7, 144.9, 161.8, 166.2.

MS (ES+): *m*/*z* = 745 [4M + 1]$^+$.

(*Z*)-2-(Isocyanomethyl)-3-(4-methylphenyl)prop-2-enenitrile (3e)

Yield: 56%; brown solid; mp 61–62 °C; R_f = 0.46 (hexanes–EtOAc, 8:2).

IR (KBr): 2151 (NC), 2213 (CN) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.43 (s, 3 H, CH_3), 4.37 (s, 2 H, CH_2), 7.28–7.30 (m, 3 H, ArH and =CH), 7.72 (d, *J* = 8.0 Hz, 2 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.8, 45.3, 101.2, 116.6, 127.6, 128.5, 129.5, 130.1, 146.3.

MS (ES+): *m*/*z* = 729 [4M + 1]$^+$.

(*Z*)-2-(Isocyanomethyl)-3-(4-methoxyphenyl)prop-2-enenitrile (3f)

Yield: 62%; yellow solid; mp 71–72 °C; R_f = 0.35 (hexanes–EtOAc, 8:2).

IR (KBr): 2151 (NC), 2217 (CN) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.87 (s, 3 H, OCH_3), 4.33 (s, 2 H, CH_2), 6.97 (dd, *J* = 2.0, 6.9 Hz, 2 H, ArH), 7.19 (s, 1 H, =CH), 7.79 (d, *J* = 8.8 Hz, 2 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 45.4, 55.7, 99.2, 114.7, 115.0, 116.9, 124.8, 131.4, 131.5, 146.0, 148.9, 162.4.

MS (ES+): *m*/*z* = 793 [4M + 1]$^+$.

(*Z*)-3-(2,4-Dichlorophenyl)-2-(isocyanomethyl)prop-2-enenitrile (3g)

Yield: 46%; yellow solid; mp 80–81 °C; R_f = 0.58 (hexanes–EtOAc, 8:2).

IR (KBr): 2152 (NC), 2224 (CN) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.42 (s, 2 H, CH_2), 7.39 (d, *J* = 8.4 Hz, 1 H, ArH), 7.51 (s, 1 H, =CH), 7.64 (s, 1 H, ArH), 7.94 (d, *J* = 8.4 Hz, 1 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 44.9, 106.6, 115.3, 128.1, 129.1, 130.1, 130.2, 135.6, 138.0, 141.7, 162.5.

MS (ES–): *m*/*z* = 707 [3M – 1]$^-$.

Substituted Imidazo[1,2-*a*]pyridines 8a–g, 9a–g, 10a,b,e and 11a; General Procedure

A soln of 2-aminopyridine (0.094 g, 1.0 mmol) and an appropriate aldehyde **4**–**7** (1.0 mmol) in toluene (15 mL) was heated for 30 min. Solid NH_4Cl (0.107 g, 2.0 mmol) and an appropriate isonitrile **3a**–**g** (1.0 mmol) were added and the reaction mixture was brought to reflux. After 5–6 h, H_2O (100 mL) was added and the mixture was extracted with EtOAc (3 × 30 mL). The organic layers were pooled, dried (anhyd Na_2SO_4) and concentrated under reduced pressure. The residue so obtained was purified by silica gel column chromatography (30–50% EtOAc–hexanes) to afford pure product in 35–68% yield.

(*Z*)-2-({[2-(4-Chlorophenyl)imidazo[1,2-*a*]pyridin-3-yl]amino}methyl)-3-phenylprop-2-enenitrile (8a)

Yield: 54%; yellow solid; mp 155–156 °C; R_f = 0.20 (hexanes–EtOAc, 7:3).

IR (KBr): 2206 (CN), 3418 (NH) cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.59 (t, *J* = 6.0 Hz, 1 H, CH_2NH), 3.93 (d, *J* = 5.5 Hz, 2 H, CH_2NH), 6.77 (s, 1 H, =CH), 6.91 (dt, *J* = 1.7, 10.2 Hz, 1 H, ArH), 7.15–7.23 (m, 1 H, ArH), 7.36–7.46 (m, 5 H, ArH), 7.52–7.58 (m, 3 H, ArH), 7.95 (dd, *J* = 2.0, 6.7 Hz, 2 H, ArH), 8.29 (d, *J* = 6.9 Hz, 1 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 53.1, 108.9, 112.4, 117.6, 118.6, 122.6, 123.6, 124.9, 128.5, 128.7, 128.8, 128.89, 128.93, 129.0, 130.8, 132.6, 132.8, 133.6, 136.7, 142.1, 145.4.

MS (ES+): *m*/*z* = 385.1 [M + 1]$^+$.

HRMS (EI): *m*/*z* calcd for $C_{23}H_{17}ClN_4$: 384.1142; found: 384.1142.

(*Z*)-3-(2-Chlorophenyl)-2-({[2-(4-chlorophenyl)imidazo[1,2-*a*]pyridin-3-yl]amino}methyl)prop-2-enenitrile (8b)

Yield: 58%; yellow solid; mp 119–120 °C; R_f = 0.22 (hexanes–EtOAc, 7:3).

IR (KBr): 2208 (CN), 3417 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.49 (t, *J* = 5.9 Hz, 1 H, CH_2NH), 3.83 (d, *J* = 5.9 Hz, 2 H, CH_2NH), 6.90 (dt, *J* = 1.0, 6.8 Hz, 1 H, ArH), 7.15 (s, 1 H, =CH), 7.19–7.25 (m, 1 H, ArH), 7.29–7.39 (m, 3 H, ArH), 7.53–7.57 (m, 2 H, ArH), 7.62 (dd, *J* = 1.3, 7.6 Hz, 1 H, ArH), 7.68 (dt, *J* = 1.9, 6.8 Hz, 1 H, ArH), 7.76 (dd, *J* = 1.4, 7.7 Hz, 1 H, ArH), 7.95 (dd, *J* = 1.1, 8.0 Hz, 1 H, ArH), 8.26 (d, *J* = 6.9 Hz, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 52.9, 110.0, 112.7, 118.0, 122.9, 123.7, 125.3, 127.5, 128.9, 129.4, 129.5, 130.1, 131.6, 131.8, 132.9, 134.0, 134.5, 142.3.

MS (ES+): *m*/*z* = 419.1 [M + 1]$^+$.

Anal. Calcd for $C_{23}H_{16}Cl_2N_4$: C, 65.88; H, 3.85; N, 13.36. Found: C, 65.66; H, 4.08; N, 13.12.

(*Z*)-3-(4-Chlorophenyl)-2-({[2-(4-chlorophenyl)imidazo[1,2-*a*]pyridin-3-yl]amino}methyl)prop-2-enenitrile (8c)

Yield: 68%; yellow solid; mp 171–172 °C; R_f = 0.22 (hexanes–EtOAc, 7:3).

IR (KBr): 2216 (CN), 3422 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.64 (s, 1 H, CH_2NH), 3.91 (d, *J* = 5.8 Hz, 2 H, CH_2NH), 6.68 (s, 1 H, =CH), 6.87 (t, *J* = 6.8 Hz, 1 H, ArH), 7.16–7.22 (m, 1 H, ArH), 7.33 (d, *J* = 8.6 Hz, 2 H, ArH), 7.41–7.48 (m, 4 H, ArH), 7.53–7.56 (m, 1 H, ArH), 7.93 (d, *J* = 8.6 Hz, 2 H, ArH), 8.25–8.27 (m, 1 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 53.1, 109.6, 112.6, 117.7, 118.5, 122.7, 123.6, 125.2, 128.6, 129.1, 129.3, 130.2, 131.3, 132.6, 133.8, 136.8, 136.9, 142.2, 144.0.

MS (ES+): *m*/*z* = 419.1 $[M + 1]^+$.

Anal. Calcd for $C_{23}H_{16}Cl_2N_4$: C, 65.88; H, 3.85; N, 13.36. Found: C, 65.95; H, 3.77; N, 13.21.

(*Z*)-2-({[2-(4-Chlorophenyl)imidazo[1,2-*a*]pyridin-3-yl]amino}methyl)-3-(4-fluorophenyl)prop-2-enenitrile (8d)
Yield: 61%; yellow solid; mp 136–137 °C; R_f = 0.35 (hexanes–EtOAc, 7:3).

IR (KBr): 2209 (CN), 3342 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.61 (t, *J* = 5.7 Hz, 1 H, CH_2NH), 3.91 (d, *J* = 5.8 Hz, 2 H, CH_2NH), 6.68 (s, 1 H, =CH), 6.86 (t, *J* = 6.7 Hz, 1 H, ArH), 7.05 (t, *J* = 8.5 Hz, 2 H, ArH), 7.19 (t, *J* = 7.8 Hz, 1 H, ArH), 7.42 (d, *J* = 8.4 Hz, 2 H, ArH), 7.54 (dd, *J* = 3.3, 6.7 Hz, 3 H, ArH), 7.93 (d, *J* = 8.4 Hz, 2 H, ArH), 8.26 (d, *J* = 6.7 Hz, 1 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.9, 108.5, 112.4, 116.0, 116.3, 117.5, 118.6, 122.6, 123.5, 125.0, 128.5, 129.0, 130.9, 131.1, 132.5, 133.6, 136.6, 142.1, 144.0, 162.2.

MS (ES+): *m*/*z* = 403.1 $[M + 1]^+$.

Anal. Calcd for $C_{23}H_{16}ClFN_4$: C, 68.57; H, 4.00; N, 13.91. Found: C, 68.55; H, 4.09; N, 13.75.

(*Z*)-2-({[2-(4-Chlorophenyl)imidazo[1,2-*a*]pyridin-3-yl]amino}methyl)-3-(4-methylphenyl)prop-2-enenitrile (8e)
Yield: 51%; yellow solid; mp 122–123 °C; R_f = 0.24 (hexanes–EtOAc, 7:3).

IR (KBr): 2213 (CN), 3368 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.36 (s, 3 H, CH_3), 3.60 (t, *J* = 5.7 Hz, 1 H, CH_2NH), 3.91 (d, *J* = 5.9 Hz, 2 H, CH_2NH), 6.73 (s, 1 H, =CH), 6.83–6.88 (m, 1 H, ArH), 7.16–7.21 (m, 3 H, ArH), 7.41–7.48 (m, 4 H, ArH), 7.54 (d, *J* = 9.1 Hz, 1 H, ArH), 7.95 (d, *J* = 8.6 Hz, 2 H, ArH), 8.28 (d, *J* = 6.9 Hz, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.7, 53.3, 107.6, 112.5, 117.6, 119.0, 122.8, 123.8, 125.1, 128.6, 129.1, 129.14, 129.8, 130.2, 132.7, 133.8, 136.6, 141.6, 142.2, 145.6.

MS (ES+): *m*/*z* = 399.1 $[M + 1]^+$.

HRMS (EI): *m*/*z* calcd for $C_{24}H_{19}ClN_4$: 398.1298; found: 398.1287.

(*Z*)-2-({[2-(4-Chlorophenyl)imidazo[1,2-*a*]pyridin-3-yl]amino}methyl)-3-(4-methoxyphenyl)prop-2-enenitrile (8f)
Yield: 63%; yellow solid; mp 165–166 °C; R_f = 0.22 (hexanes–EtOAc, 7:3).

IR (KBr): 2203 (CN), 3344 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.57 (t, *J* = 6.0 Hz, 1 H, CH_2NH), 3.83 (s, 3 H, OCH_3), 3.88 (d, *J* = 5.6 Hz, 2 H, CH_2NH), 6.67 (s, 1 H, =CH), 6.82–6.90 (m, 3 H, ArH), 7.14–7.20 (m, 1 H, ArH), 7.40–7.44 (m, 2 H, ArH), 7.52–7.57 (m, 3 H, ArH), 7.94 (dd, *J* = 1.9, 6.7 Hz, 2 H, ArH), 8.26–8.28 (m, 1 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 53.3, 55.6, 105.7, 112.5, 114.4, 117.6, 119.3, 122.8, 123.9, 125.0, 125.7, 128.6, 129.1, 130.9, 132.8, 133.7, 136.6, 142.2, 145.1, 161.7.

MS (ES+): *m*/*z* = 415.1 $[M + 1]^+$.

Anal. Calcd for $C_{24}H_{19}ClN_4O$: C, 69.48; H, 4.62; N, 13.50. Found: C, 69.64; H, 4.49; N, 13.21.

(*Z*)-2-({[2-(4-Chlorophenyl)imidazo[1,2-*a*]pyridin-3-yl]amino}methyl)-3-(2,4-dichlorophenyl)prop-2-enenitrile (8g)
Yield: 52%; yellow solid; mp 151–152 °C; R_f = 0.20 (hexanes–EtOAc, 7:3).

IR (KBr): 2205 (CN), 3380 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.69 (s, 1 H, CH_2NH), 3.95 (d, *J* = 4.2 Hz, 2 H, CH_2NH), 6.88 (s, 1 H, ArH), 7.02 (s, 1 H, =CH), 7.38–7.45 (m, 4 H, ArH), 7.56 (d, *J* = 8.4 Hz, 3 H, ArH), 7.95 (d, *J* = 7.5 Hz, 2 H, ArH), 8.25 (d, *J* = 5.1 Hz, 1 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.7, 112.6, 113.1, 117.8, 122.7, 123.4, 125.2, 127.8, 128.7, 129.2, 129.9, 132.6, 133.9, 135.1, 137.1, 140.9, 142.3.

MS (ES+): *m*/*z* = 453.1 $[M + 1]^+$.

HRMS (EI): *m*/*z* calcd for $C_{23}H_{15}Cl_3N_4$: 452.0363; found: 452.0395.

(*Z*)-2-({[2-(2-Nitrophenyl)imidazo[1,2-*a*]pyridin-3-yl]amino}methyl)-3-phenylprop-2-enenitrile (9a)
Yield: 55%; yellow solid; mp 129–131 °C; R_f = 0.15 (hexanes–EtOAc, 7:3).

IR (KBr): 2209 (CN), 3373 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.48 (t, *J* = 6.1 Hz, 1 H, CH_2NH), 3.79 (d, *J* = 5.9 Hz, 2 H, CH_2NH), 6.76 (s, 1 H, =CH), 6.89 (t, *J* = 6.6 Hz, 1 H, ArH), 7.20 (t, *J* = 7.4 Hz, 1 H, ArH), 7.34–7.37 (m, 3 H, ArH), 7.46–7.62 (m, 5 H, ArH), 7.68–7.71 (m, 1 H, ArH), 7.89 (d, *J* = 7.2 Hz, 1 H, ArH), 8.25 (d, *J* = 6.9 Hz, 1 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 53.1, 108.8, 112.6, 118.0, 118.3, 122.7, 124.4, 124.8, 124.9, 128.8, 128.9, 129.0, 130.7, 132.58, 132.64, 132.9, 134.5, 142.2, 145.3, 149.5.

MS (ES+): *m*/*z* = 396.1 $[M + 1]^+$.

HRMS (EI): *m*/*z* calcd for $C_{23}H_{17}N_5O_2$: 395.1382; found: 395.1346.

(*Z*)-3-(2-Chlorophenyl)-2-({[2-(2-nitrophenyl)imidazo[1,2-*a*]pyridin-3-yl]amino}methyl)prop-2-enenitrile (9b)
Yield: 51%; yellow solid; mp 122–123 °C; R_f = 0.25 (hexanes–EtOAc, 7:3).

IR (KBr): 2216 (CN), 3348 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.65 (t, *J* = 5.9 Hz, 1 H, CH_2NH), 3.99 (d, *J* = 5.9 Hz, 2 H, CH_2NH), 6.89 (t, *J* = 6.3 Hz, 1 H, ArH), 7.16 (s, 1 H, =CH), 7.22 (dt, *J* = 1.1, 7.9 Hz, 1 H, ArH), 7.30–7.34 (m, 2 H, ArH), 7.36–7.40 (m, 1 H, ArH), 7.47 (d, *J* = 8.6 Hz, 2 H, ArH), 7.58 (d, *J* = 9.0 Hz, 1 H, ArH), 7.66–7.69 (m, 1 H, ArH), 7.99 (d, *J* = 8.6 Hz, 2 H, ArH), 8.29 (d, *J* = 6.8 Hz, 1 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 51.8, 111.8, 112.0, 116.8, 117.3, 122.0, 124.1, 124.2, 126.4, 128.2, 128.3, 129.1, 130.6, 130.8, 131.9, 133.5, 133.7, 141.0, 141.5.

MS (ES+): *m*/*z* = 430.1 $[M + 1]^+$.

HRMS (EI): *m*/*z* calcd for $C_{23}H_{16}ClN_5O_2$: 429.0993; found: 429.0972.

(*Z*)-3-(4-Chlorophenyl)-2-({[2-(2-nitrophenyl)imidazo[1,2-*a*]pyridin-3-yl]amino}methyl)prop-2-enenitrile (9c)
Yield: 50%; yellow viscous oil; R_f = 0.20 (hexanes–EtOAc, 7:3).

IR (neat): 2215 (CN), 3347 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.52 (t, *J* = 4.3 Hz, 1 H, CH_2NH), 3.79 (d, *J* = 4.3 Hz, 2 H, CH_2NH), 6.71 (s, 1 H, =CH), 6.89 (t, *J* = 5.1 Hz, 1 H, ArH), 7.43–7.48 (m, 4 H, ArH), 7.62–7.69 (m, 3 H, ArH), 7.84 (d, *J* = 6.4 Hz, 2 H, ArH), 8.11 (d, *J* = 5.9 Hz, 1 H, ArH), 8.24 (d, *J* = 5.1 Hz, 1 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.9, 109.3, 112.7, 117.9, 122.7, 124.4, 125.0, 128.7, 128.9, 129.1, 129.6, 130.1, 131.2, 131.3, 132.5, 132.6, 134.4, 136.6, 142.2, 143.9, 149.4.

MS (ES+): *m*/*z* = 430.1 $[M + 1]^+$.

HRMS (EI): *m*/*z* calcd for $C_{23}H_{16}ClN_5O_2$: 429.0993; found: 429.0986.

(*Z*)-3-(4-Fluorophenyl)-2-({[2-(2-nitrophenyl)imidazo[1,2-*a*]pyridin-3-yl]amino}methyl)prop-2-enenitrile (9d)
Yield: 45%; yellow viscous oil; R_f = 0.19 (hexanes–EtOAc, 7:3).

IR (neat): 2215 (CN), 3375 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.51 (s, 1 H, CH_2NH), 3.78 (d, *J* = 5.0 Hz, 2 H, CH_2NH), 6.71 (s, 1 H, =CH), 6.89 (d, *J* = 6.1 Hz, 2 H, ArH), 7.00–7.06 (m, 3 H, ArH), 7.53–7.58 (m, 5 H, ArH), 7.89 (d, *J* = 8.2 Hz, 1 H, ArH), 8.24 (d, *J* = 6.6 Hz, 1 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 53.1, 108.4, 112.8, 116.0, 116.3, 118.0, 118.4, 122.8, 124.6, 124.8, 125.2, 128.8, 129.1, 131.1, 131.2, 132.7, 132.8, 142.3, 144.2.

MS (ES+): *m*/*z* = 414.1 $[M + 1]^+$.

HRMS (EI): *m*/*z* calcd for $C_{23}H_{16}FN_5O_2$: 413.1288; found: 413.1289.

(*Z*)-3-(4-Methylphenyl)-2-({[2-(2-nitrophenyl)imidazo[1,2-*a*]pyridin-3-yl]amino}methyl)prop-2-enenitrile (9e)
Yield: 55%; yellow viscous oil; R_f = 0.30 (hexanes–EtOAc, 7:3).

IR (neat): 2212 (CN), 3385 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.38 (s, 3 H, CH_3), 3.49 (t, *J* = 5.7 Hz, 1 H, CH_2NH), 3.79 (d, *J* = 5.5 Hz, 2 H, CH_2NH), 6.73 (s, 1 H, =CH), 6.87–6.92 (m, 1 H, ArH), 7.16–7.18 (m, 2 H, ArH), 7.45–7.56 (m, 5 H, ArH), 7.62 (dt, *J* = 1.3, 7.5 Hz, 1 H, ArH), 7.71 (dd, *J* = 1.4, 7.6 Hz, 1 H, ArH), 7.91 (dd, *J* = 1.1, 8.1 Hz, 1 H, ArH), 8.27 (d, *J* = 6.8 Hz, 1 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.7, 53.3, 107.5, 112.7, 118.1, 118.6, 122.8, 124.6, 124.9, 125.1, 129.0, 129.1, 129.7, 130.3, 132.7, 132.8, 141.4, 142.3, 145.5.

MS (ES+): *m*/*z* = 410.1 $[M + 1]^+$.

HRMS (EI): *m*/*z* calcd for $C_{24}H_{19}N_5O_2$: 409.1539; found: 409.1537.

(*Z*)-3-(4-Methoxyphenyl)-2-({[2-(2-nitrophenyl)imidazo[1,2-*a*]pyridin-3-yl]amino}methyl)prop-2-enenitrile (9f)
Yield: 43%; yellow viscous oil; R_f = 0.21 (hexanes–EtOAc, 7:3).

IR (neat): 2211 (CN), 3384 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.47 (t, *J* = 5.9 Hz, 1 H, CH_2NH), 3.76 (d, *J* = 5.8 Hz, 2 H, CH_2NH), 3.83 (s, 3 H, OCH_3), 6.66 (s, 1 H, =CH), 6.84–6.88 (m, 3 H, ArH), 7.16–7.22 (m, 1 H, ArH), 7.49–7.54 (m, 4 H, ArH), 7.57–7.63 (m, 1 H, ArH), 7.69 (dd, *J* = 1.3, 7.6 Hz, 1 H, ArH), 7.89 (dd, *J* = 1.0, 8.0 Hz, 1 H, ArH), 8.25 (d, *J* = 6.9 Hz, 1 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 53.3, 55.6, 105.6, 112.7, 114.3, 118.0, 119.0, 122.9, 124.6, 125.0, 125.1, 125.7, 129.0, 131.0, 132.7, 134.5, 142.3, 145.1, 149.5, 161.6.

MS (ES+): *m*/*z* = 426.1 $[M + 1]^+$.

HRMS (EI): *m*/*z* calcd for $C_{24}H_{19}N_5O_3$: 425.1488; found: 425.1492.

(*Z*)-3-(2,4-Dichlorophenyl)-2-({[2-(2-nitrophenyl)imidazo[1,2-*a*]pyridin-3-yl]amino}methyl)prop-2-enenitrile (9g)
Yield: 40%; yellow viscous oil; R_f = 0.25 (hexanes–EtOAc, 7:3).

IR (neat): 2214 (CN), 3381 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.49 (t, *J* = 5.7 Hz, 1 H, CH_2NH), 3.83 (d, *J* = 5.8 Hz, 2 H, CH_2NH), 6.88–6.93 (m, 1 H, ArH), 7.06 (s, 1 H, =CH), 7.39 (d, *J* = 2.1 Hz, 1 H, ArH), 7.54–7.57 (m, 3 H, ArH), 7.60–7.67 (m, 2 H, ArH), 7.73–7.74 (m, 2 H, ArH), 7.94 (dd, *J* = 1.1, 8.0 Hz, 1 H, ArH), 8.23–8.26 (m, 1 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.6, 112.9, 113.1, 117.5, 118.1, 122.8, 124.7, 124.8, 125.2, 127.7, 129.2, 129.9, 132.8, 135.1, 137.0, 140.6, 149.6.

MS (ES+): *m*/*z* = 464.2 $[M + 1]^+$.

HRMS (EI): *m*/*z* calcd for $C_{23}H_{15}Cl_2N_5O_2$: 463.0603; found: 463.0602.

(*Z*)-2-({[2-(2-Chloro-5-nitrophenyl)imidazo[1,2-*a*]pyridin-3-yl]amino}methyl)-3-phenylprop-2-enenitrile (10a)
Yield: 50%; yellow solid; mp 131–132 °C; R_f = 0.21 (hexanes–EtOAc, 7:3).

IR (KBr): 2205 (CN), 3380 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.76 (s, 3 H, CH_2NH and CH_2NH), 6.49 (s, 1 H, =CH), 6.95 (t, *J* = 6.5 Hz, 1 H, ArH), 7.27–7.37 (m, 4 H, ArH), 7.42 (d, *J* = 6.8 Hz, 2 H, ArH), 7.60 (d, *J* = 9.1 Hz, 1 H, ArH), 7.64 (d, *J* = 8.8 Hz, 1 H, ArH), 8.09 (dd, *J* = 2.7, 8.8 Hz, 1 H, ArH), 8.31 (d, *J* = 6.8 Hz, 1 H, ArH), 8.34 (d, *J* = 2.7 Hz, 1 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 53.4, 108.2, 112.9, 118.1, 122.8, 123.9, 125.0, 125.4, 127.5, 128.8, 129.0, 131.0, 131.2, 132.5, 134.8, 135.3, 139.3, 142.6, 145.4, 146.5.

MS (ES+): *m*/*z* = 430.1 $[M + 1]^+$.

HRMS (EI): *m*/*z* calcd for $C_{23}H_{16}ClN_5O_2$: 429.0993; found: 429.0967.

(*Z*)-2-({[2-(2-Chloro-5-nitrophenyl)imidazo[1,2-*a*]pyridin-3-yl]amino}methyl)-3-(2-chlorophenyl)prop-2-enenitrile (10b)
Yield: 35%; yellow solid; mp 162–163 °C; R_f = 0.31 (hexanes–EtOAc, 7:3).

IR (KBr): 2205 (CN), 3385 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.81 (br s, 3 H, CH_2NH and CH_2NH), 6.93–6.97 (m, 2 H, ArH and =CH), 7.20–7.38 (m, 4 H, ArH), 7.59–7.68 (m, 3 H, ArH), 8.12–8.15 (m, 1 H, ArH), 8.31 (d, *J* = 6.8 Hz, 1 H, ArH), 8.47 (d, *J* = 2.2 Hz, 1 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.7, 111.6, 112.8, 117.1, 118.0, 122.7, 123.9, 124.8, 125.2, 127.1, 127.5, 128.5, 129.9, 130.7, 130.9, 131.7, 134.2, 134.5, 135.2, 139.2, 141.5, 142.5, 146.5.

MS (ES+): *m*/*z* = 464.1 $[M + 1]^+$.

Anal. Calcd for $C_{23}H_{15}Cl_2N_5O_2$: C, 59.50; H, 3.26; N, 15.08. Found: C, 59.69; H, 3.45; N, 14.84.

(*Z*)-2-({[2-(2-Chloro-5-nitrophenyl)imidazo[1,2-*a*]pyridin-3-yl]amino}methyl)-3-(4-methylphenyl)prop-2-enenitrile (10e)
Yield: 40%; yellow solid; mp 162–163 °C; R_f = 0.25 (hexanes–EtOAc, 7:3).

IR (KBr): 2212 (CN), 3282 (NH) cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.35 (s, 3 H, CH_3), 3.70–3.80 (m, 3 H, CH_2NH and CH_2NH), 6.40 (s, 1 H, =CH), 6.95 (dt, *J* = 0.8, 6.8 Hz, 1 H, ArH), 7.19 (d, *J* = 8.2 Hz, 2 H, ArH), 7.24–7.29 (m, 2 H, ArH), 7.33 (s, 1 H, ArH), 7.62 (t, *J* = 8.5 Hz, 2 H, ArH), 8.07 (dd, *J* = 2.8, 8.8 Hz, 1 H, ArH), 8.29–8.32 (m, 2 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.5, 53.3, 106.6, 112.7, 118.0, 118.1, 122.7, 123.8, 124.9, 125.2, 127.4, 128.7, 129.5, 129.7, 130.8, 134.7, 135.2, 139.0, 141.9, 142.5, 145.3, 146.4.

MS (ES+): *m*/*z* = 444.1 $[M + 1]^+$.

Anal. Calcd for $C_{24}H_{18}ClN_5O_2$: C, 64.94; H, 4.09; N, 15.78. Found: C, 64.77; H, 4.02; N, 15.91.

(*Z*)-3-Phenyl-2-({[2-(5-phenylisoxazol-3-yl)imidazo[1,2-*a*]pyridin-3-yl]amino}methyl)prop-2-enenitrile (11a)
Yield: 36%; yellow solid; mp 145–146 °C; R_f = 0.30 (hexanes–EtOAc, 7:3).

IR (KBr): 2213 (CN), 3338 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.09 (s, 3 H, CH_2NH and CH_2NH), 6.93–6.95 (m, 1 H, ArH), 7.11 (s, 1 H, ArH), 7.17 (s, 1 H, ArH), 7.41–7.58 (m, 8 H, ArH), 7.73 (s, 2 H, ArH), 7.89 (s, 2 H, ArH), 8.41 (d, *J* = 6.0 Hz, 1 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 53.9, 99.3, 108.8, 113.1, 117.8, 123.1, 126.0, 126.9, 127.2, 128.9, 128.97, 129.0, 130.2, 130.8, 132.8, 142.6, 145.7.

MS (ES+): *m*/*z* = 418.2 $[M + 1]^+$.

Anal. Calcd for $C_{26}H_{19}N_5O$: C, 74.80; H, 4.59; N, 16.78. Found: C, 74.99; H, 4.45; N, 16.76.

(*Z*)-2-[(6-Amino-5,7,8,13-tetraazadibenzo[*a*,*e*]azulen-7-yl)methyl]-3-phenylprop-2-enenitrile (13a); Typical Procedure for the Synthesis of Compounds 13a–g
To a soln of **9a** (0.2 g, 0.50 mmol) in a mixture of THF–H_2O (8.0 mL, 1:1), In powder (0.176 g, 1.52 mmol) was added followed by the dropwise addition of concd HCl (0.24 mL), and the reaction mixture was allowed to stir at r.t. for 1 h. On completion, the THF was removed, EtOAc (10 mL) was added to the residue and the solution was neutralized with sat. $NaHCO_3$ soln. The mixture was passed through a Celite® bed with EtOAc. The organic layer was separated and the aqueous layer was further extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with brine, dried (anhyd Na_2SO_4) and concentrated to yield the crude product. The crude product was dissolved in THF (6.0 mL) and then BrCN (0.078 g, 0.74 mmol) and K_2CO_3 (0.136 g, 0.98 mmol) were simultaneously added, and the reaction mixture was allowed to stir for 9 h. After completion, the solvent was removed under reduced pressure to provide the crude product, which upon column chromatography on silica gel (MeOH–EtOAc, 1:4) afforded **13a** as a yellow solid; yield: 0.120 g (62%); mp 220–221 °C; R_f = 0.20 (EtOAc–MeOH, 8:2).

IR (KBr): 2208 (CN), 3417 (NH_2) cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 4.15 (d, *J* = 3.3 Hz, 2 H, CH_2), 6.56 (s, 1 H, ArH), 7.44–7.53 (m, 6 H, ArH and =CH), 7.61–7.73 (m, 4 H, ArH and NH_2), 7.99 (s, 1 H, ArH), 8.27 (t, *J* = 8.1 Hz, 1 H, ArH), 8.67 (s, 1 H, ArH), 8.92 (d, *J* = 7.7 Hz, 1 H, ArH), 9.20 (s, 1 H, ArH).

MS (ES+): *m*/*z* = 391.1 $[M + 1]^+$.

HRMS (EI): *m*/*z* calcd for $C_{24}H_{18}N_6$: 390.1593; found: 390.1574.

(*Z*)-2-[(6-Amino-5,7,8,13-tetraazadibenzo[*a*,*e*]azulen-7-yl)methyl]-3-(2-chlorophenyl)prop-2-enenitrile (13b)
Yield: 61%; yellow solid; mp 231–232 °C; R_f = 0.28 (EtOAc–MeOH, 8:2).

IR (KBr): 2202 (CN), 3431 (NH_2) cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 4.23 (d, *J* = 5.6 Hz, 2 H, CH_2), 6.56 (t, *J* = 5.5 Hz, 1 H, ArH), 7.42–7.52 (m, 7 H, ArH, =CH and NH_2), 7.62–7.68 (m, 2 H, ArH), 8.00 (t, *J* = 6.8 Hz, 1 H, ArH), 8.30 (t, *J* = 8.1 Hz, 1 H, ArH), 8.66 (d, *J* = 7.4 Hz, 1 H, ArH), 9.02 (br s, 1 H, ArH), 9.18 (d, *J* = 6.5 Hz, 1 H, ArH).

MS (ES+): *m*/*z* = 425.2 $[M + 1]^+$.

HRMS (EI): *m*/*z* calcd for $C_{24}H_{17}ClN_6$: 424.1203; found: 424.1205.

(*Z*)-2-[(6-Amino-5,7,8,13-tetraazadibenzo[*a*,*e*]azulen-7-yl)methyl]-3-(4-chlorophenyl)prop-2-enenitrile (13c)
Yield: 70%; yellow solid; mp 210–211 °C; R_f = 0.32 (EtOAc–MeOH, 8:2).

IR (KBr): 2208 (CN), 3424 (NH_2) cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 4.14 (s, 2 H, CH_2), 6.63 (s, 1 H, ArH), 7.49–7.56 (m, 5 H, ArH and =CH), 7.63–7.66 (m, 4 H, ArH and NH_2), 7.99 (s, 1 H, ArH), 8.28 (t, *J* = 8.0 Hz, 1 H, ArH), 8.68 (d, *J* = 5.6 Hz, 1 H, ArH), 8.95 (d, *J* = 7.4 Hz, 1 H, ArH), 9.25 (s, 1 H, ArH).

MS (ES+): *m*/*z* = 425.2 $[M + 1]^+$.

HRMS (EI): *m*/*z* calcd for $C_{24}H_{17}ClN_6$: 424.1203; found: 424.1198.

(*Z*)-2-[(6-Amino-5,7,8,13-tetraazadibenzo[*a*,*e*]azulen-7-yl)methyl]-3-(4-fluorophenyl)prop-2-enenitrile (13d)
Yield: 69%; yellow solid; mp 227–228 °C; R_f = 0.26 (EtOAc–MeOH, 8:2).

IR (KBr): 2208 (CN), 3411 (NH_2) cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 4.13 (d, *J* = 5.5 Hz, 2 H, CH_2), 6.47 (s, 1 H, ArH), 7.28–7.44 (m, 4 H, ArH and =CH), 7.67–7.71 (m, 5 H, ArH and NH_2), 7.98 (s, 1 H, ArH), 8.29 (d, *J* = 7.9 Hz, 1 H, ArH), 8.65 (d, *J* = 4.7 Hz, 1 H, ArH), 8.93 (s, 1 H, ArH), 9.19 (m, 1 H, ArH).

MS (ES+): *m*/*z* = 409.2 $[M + 1]^+$.

HRMS (EI): *m*/*z* calcd for $C_{24}H_{17}FN_6$: 408.1499; found: 408.1501.

(*Z*)-2-[(6-Amino-5,7,8,13-tetraazadibenzo[*a*,*e*]azulen-7-yl)methyl]-3-(4-methylphenyl)prop-2-enenitrile (13e)
Yield: 73%; yellow solid; mp 218–219 °C; R_f = 0.35 (EtOAc–MeOH, 8:2).

IR (KBr): 2207 (CN), 3401 (NH_2) cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.33 (s, 3 H, CH_3), 4.14 (s, 2 H, CH_2), 6.46 (s, 1 H, ArH), 7.25–7.28 (m, 2 H, ArH), 7.40–7.70 (m, 7 H, ArH, =CH and NH_2), 7.99 (s, 1 H, ArH), 8.27 (t, *J* = 7.5 Hz, 1 H, ArH), 8.68 (d, *J* = 7.8 Hz, 1 H, ArH), 8.90 (d, *J* = 9.6 Hz, 1 H, ArH), 9.18 (s, 1 H, ArH).

MS (ES+): *m*/*z* = 405.2 $[M + 1]^+$.

HRMS (EI): *m*/*z* calcd for $C_{25}H_{20}N_6$: 404.1750; found: 404.1732.

(*Z*)-2-[(6-Amino-5,7,8,13-tetraazadibenzo[*a*,*e*]azulen-7-yl)methyl]-3-(4-methoxyphenyl)prop-2-enenitrile (13f)
Yield: 72%; yellow solid; mp 209–210 °C; R_f = 0.31 (EtOAc–MeOH, 8:2).

IR (KBr): 2208 (CN), 3417 (NH_2) cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.80 (s, 3 H, OCH_3), 4.10 (s, 2 H, CH_2), 6.97–7.03 (m, 4 H, ArH and =CH), 7.37–7.66 (m, 6 H, ArH and NH_2), 7.88–7.97 (m, 2 H, ArH), 8.28 (d, *J* = 6.1 Hz, 1 H, ArH), 8.66–8.73 (m, 1 H, ArH), 9.21 (s, 1 H, ArH).

MS (ES+): *m*/*z* = 421.2 $[M + 1]^+$.

HRMS (EI): *m*/*z* calcd for $C_{25}H_{20}N_6O$: 420.1698; found: 420.1699.

(*Z*)-2-[(6-Amino-5,7,8,13-tetraazadibenzo[*a*,*e*]azulen-7-yl)methyl]-3-(2,4-dichlorophenyl)prop-2-enenitrile (13g)
Yield: 66%; yellow solid; mp 224–225 °C; R_f = 0.29 (EtOAc–MeOH, 8:2).

IR (KBr): 2215 (CN), 3422 (NH_2) cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 4.22 (d, *J* = 5.8 Hz, 2 H, CH_2), 6.52 (t, *J* = 5.6 Hz, 1 H, ArH), 7.42–7.55 (m, 4 H, ArH and =CH), 7.63–7.72 (m, 4 H, ArH and NH_2), 7.99 (t, *J* = 7.0 Hz, 1 H, ArH),

8.29 (t, J = 8.1 Hz, 1 H, ArH), 8.63 (d, J = 7.5 Hz, 1 H, ArH), 8.96 (s, 1 H, ArH), 9.15 (d, J = 6.3 Hz, 1 H, ArH).

MS (ES+): m/z = 459.1 $[M + 1]^+$.

HRMS (EI): m/z calcd for $C_{24}H_{16}Cl_2N_6$: 458.0813; found: 458.0804.

Acknowledgment

One of the authors (M.N.) gratefully acknowledges financial support from the Council of Scientific and Industrial Research, N. Delhi in the form of a fellowship. This work was accomplished under a DST, N. Delhi funded project (SR/SI/OC-16/2006).

References

(1) CDRI Communication No. 7599.
(2) Singh, V.; Batra, S. *Tetrahedron* **2008**, *64*, 4511.
(3) Pathak, R.; Singh, V.; Nag, S.; Kanojiya, S.; Batra, S. *Synthesis* **2006**, 813.
(4) (a) Pathak, R.; Batra, S. *Tetrahedron* **2007**, *63*, 9448. (b) Nag, S.; Madapa, S.; Batra, S. *Synthesis* **2008**, 101. (c) Nag, S.; Mishra, A.; Batra, S. *Tetrahedron* **2008**, *64*, 10162.
(5) For a few examples only, see: (a) Dömling, A.; Ugi, I. *Angew. Chem. Int. Ed.* **2000**, *39*, 3168; and references cited therein. (b) Dömling, A. *Chem. Rev.* **2006**, *106*, 17; and references cited therein. (c) Nair, V.; Rajesh, C.; Vinod, A. U.; Bindu, S.; Sreekanth, A. R.; Mathen, J. S.; Balagopal, L. *Acc. Chem. Res.* **2003**, *36*, 899. (d) Akritopoulou-Zanze, I. *Curr. Opin. Chem. Biol.* **2008**, *12*, 324; and references cited therein.
(6) (a) Hulme, C.; Lee, Y.-S. *Mol. Diversity* **2008**, *12*, 1; and references cited therein. (b) Parchinsky, V. Z.; Shuvalova, O.; Ushakova, O.; Kravchenko, D. V.; Krasavin, M. *Tetrahedron Lett.* **2006**, *47*, 947. (c) DiMauro, E. F.; Kennedy, J. M. *J. Org. Chem.* **2007**, *72*, 1013. (d) Tu, S.; Li, C.; Li, G.; Cao, L.; Shao, Q.; Zhou, D.; Jiang, B.; Zhou, J.; Xia, M. *J. Comb. Chem.* **2007**, *9*, 1144. (e) Shaabani, A.; Rezazadeh, F.; Soleimani, E. *Monatsh. Chem.* **2008**, *139*, 931.
(7) For a few recent examples only, see: (a) Enguehard-Gueiffier, C.; Gueiffier, A. *Mini-Rev. Med. Chem.* **2007**, *7*, 888. (b) Imaeda, Y.; Kawamoto, T.; Tobisu, M.; Konishi, N.; Hiroe, K.; Kawamura, M.; Tanaka, T.; Kubo, K. *Bioorg. Med. Chem.* **2008**, *16*, 3125. (c) Rether, J.; Erkel, G.; Anke, T.; Bajtner, J.; Sterner, O. *Bioorg. Med. Chem.* **2008**, *16*, 1236. (d) Buckley, G. M.; Fosbeary, R.; Fraser, J. L.; Gowers, L.; Higueruelo, A. P.; James, L. A.; Jenkins, K.; Mack, S. R.; Morgan, T.; Parry, D. M.; Pitt, W. R.; Rausch, O.; Richard, M. D.; Sabin, V. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 3656. (e) Buckley, G. M.; Ceska, T. A.; Fraser, J. L.; Gowers, L.; Groom, C. R.; Higueruelo, A. P.; Jenkins, K.; Mack, S. R.; Morgan, T.; Parry, D. M.; Pitt, W. R.; Rausch, O.; Richard, M. D.; Sabin, V. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 3291. (f) Ismail, M. A.; Arafa, R. K.; Wenzler, T.; Brun, R.; Tanious, F. A.; Wilson, W. D.; Boykin, D. W. *Bioorg. Med. Chem.* **2008**, *16*, 683. (g) Zimmermann, P. J.; Buhr, W.; Brehm, C.; Palmer, A. M.; Feth, M. P.; Senn-Bilfinger, J.; Simon, W.-A. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 5374. (h) Gudmundsson, K. S.; Johns, B. A. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 2735. (i) Scribner, A.; Dennis, R.; Hong, J.; Lee, S.; McIntyre, D.; Perrey, D.; Feng, D.; Fisher, M.; Wyvratt, M.; Leavitt, P.; Liberator, P.; Gurnett, A.; Brown, C.; Mathew, J.; Thompson, D.; Schmatz, D.; Biftu, T. *Eur. J. Med. Chem.* **2007**, *42*, 1334. (j) Cai, D.; Byth, K. F.; Shapiro, G. I. *Cancer Res.* **2006**, *66*, 435.