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A Facile Construction of 6-(Arylmethyl)imidazo[1,2-*a*]pyrimidin-7-ylamines from Allylamines Derived from Baylis–Hillman Adducts[‡]

Somnath Nag,[a] Amita Mishra,[a] and Sanjay Batra*[a]

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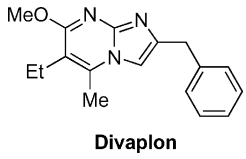
A facile and convenient synthesis of substituted imidazo[1,2-*a*]pyrimidin-7-ylamines from the allylamine derivatives afforded by the Baylis–Hillman acetates of substituted benzaldehydes and heterocyclic aldehydes by treatment with cyanamide is described. Interestingly, the allylamines afforded by heterocyclic aldehydes, which undergo fast Baylis–Hillman reaction, were discovered to undergo a one-pot reaction, whereas allylamines derived from all other aldehydes reacted by a two-step procedure.

Introduction

Pyrimidine-fused systems are of immense significance in medicinal chemistry owing to their wide range of biological activities.[1] From the broad spectrum of pyrimidine-annulated heterocycles, imidazo[1,2-*a*]pyrimidine has been an attractive target for synthetic chemists, because compounds related to this scaffold are ligands for $GABA_A$ receptors,[2] benzodiazepine receptor agonists,[3] COX-2 inhibitors[4] and anticancer,[5] antimicrobial,[6] antibacterial[7] and antifungal[8] agents. Imidazo[1,2-*a*]pyrimidine also forms the core unit of the drug Divaplon (Figure 1).[9]



Divaplon

Figure 1. Structure of Divaplon.

The synthetic application of Baylis–Hillman derivatives for achieving diverse molecular frameworks have been a progressive feature of synthetic organic chemistry during the past decade.[10] In particular, highly substituted allylamines afforded by Baylis–Hillman chemistry are excellent starting substrates for the construction of a variety of nitrogen-containing heterocyclic and fused heterocyclic systems.[10a] As a part of our continuing interest in the synthesis of heterocycles employing Baylis–Hillman chemistry, we envisaged the synthesis of imidazo[1,2-*a*]pyrimidin-7-ylamines from appropriately substituted allylamines afforded from the adducts of different aldehydes and acrylonitrile. Indeed our approach was inspired by literature reports in which the synthesis of imidazole was achieved from the reaction between imidates and α-amino acetals.[11] The retrosynthetic analysis delineated in Figure 2 explains our strategy. Cleavage of the pyrimidine ring of imidazo[1,2-*a*]-pyrimidin-7-ylamine **IV** gives the 1-substituted-2-aminoimidazole **III**. This aminoimidazole in turn could be readily generated from the allylamine **I** by reaction with cyanamide by the initial formation of the intermediate **II**. The starting secondary allylamine in turn could readily be synthesized from the S_N2' displacement reaction between 2,2-dimethoxyethylamine (aminoacetaldehyde dimethyl acetal) and the acetate afforded by the Baylis–Hillman adduct of acrylonitrile.

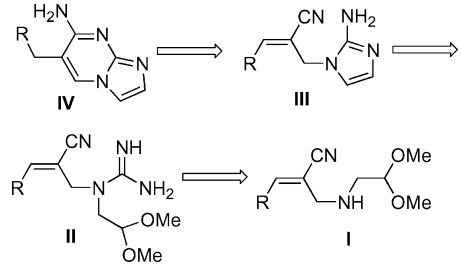


Figure 2. Retrosynthetic analysis for the synthesis of imidazo[1,2-*a*]pyrimidin-7-ylamine.

A study of the literature revealed that despite several elegant strategies[12] being known for the synthesis of imidazo[1,2-*a*]pyrimidines bearing various substituents at different positions of the ring the procedure we envisioned was a novel method. Notably, however, the CNS activity of imidazo[1,2-*a*]pyrimidin-7-ylamines has been reported previously.[13] Nevertheless, we continued with our efforts in

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[a] Medicinal and Process Chemistry Division, Central Drug Research Institute,
P. O. Box 173, Lucknow 226001, India
Fax: +91-522-2623405, -2623938
E-mail: batra_san@yahoo.co.uk

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this field, and during the course of the study we discovered that the allylamines synthesized from the Baylis–Hillman adducts of simple benzaldehydes provided the final compounds in two steps, whereas the allylamines derived from the adducts of heterocyclic aldehydes undergoing fast Baylis–Hillman reaction afforded the title compounds in a one-pot reaction. The successful results of this work are reported herein.

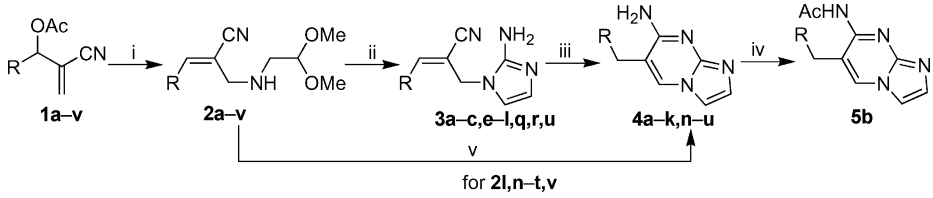
Results and Discussion

In our initial investigations we found that the Baylis–Hillman acetate **1a** reacted with 3.0 equiv. of 2,2-dimethoxyethylamine in methanol to yield the desired allylamine **2a** in 87% yield. The use of 3.0 equiv. of amine was actually guided by our earlier observation that 1.0 equiv. of primary amine during S_N2' reactions generally leads to a mixture of secondary and tertiary allylamines.[14] Under optimized conditions, compound **2a** was first treated with cyanamide in aqueous acetic acid under heating at 90–100 °C for 2 h followed by HCl and further heating for 5 min (Scheme 1). The reaction mixture was cooled, diluted with water and neutralized with sodium hydrogen carbonate. Workup and subsequent purification of the crude mixture by column chromatography led to the isolation of the product in good yield. The isolated product was identified spectroscopically as **3a** instead of the anticipated product **4a**. This implied that the second nucleophilic attack of the amino group at the 2-position of the imidazole on the nitrile group of the intended cascade sequence did not take place under our experimental conditions. As a result we extended the time of treatment with HCl beyond 5 min, monitoring the reaction for 24 h, but no change in the formation of the product was observed. With the knowledge that the desired cyclization reaction between the amino and the nitrile group followed by isomerization of the benzylidene double bond from an exocyclic to an endocyclic position can also be affected in the presence of base,[15] we evaluated different bases to find out if the desired cyclization was achievable. We were pleased to observe that the reaction of **3a** with sodium methoxide in methanol at reflux for 1 h smoothly furnished the required product 6-benzylimidazo[1,2-*a*]pyrimidin-7-ylamine (**4a**) in 76% yield. The formation of **4a** was conclusively confirmed from the IR spectrum, which displayed the loss of the signal arising from the nitrile group. Notably, it was discovered that the product **4a** could be readily identified by the presence of a characteristic blue fluorescent spot during TLC analysis. Encouraged by this result we subjected amines **2b–k** to a similar sequence to obtain **4b–k** in good yields (Table 1). However, the product **3d** generated from **1d** failed to produce the corresponding imidazo[1,2-*a*]pyrimidin-7-ylamine **4d**, instead giving a mixture of inseparable products (Table 1, Entry 4). In order to confirm the presence of the free amino group in the product, a representative compound, **4b**, was treated with acetic anhydride in the presence of pyridine. The reaction was complete in 3 h, affording the anticipated acetylated derivative **5b**.

Table 1. Yields of compounds **2**–**4** synthesized from substituted benzaldehydes.

Entry	Compd. no.	R	Yield [%]		
			2	**3**	**4**
1	**a**	C_6H_5	87	65	72
2	**b**	2-Cl-C_6H_4	95	69	78
3	**c**	2-F-C_6H_4	89	67	70
4	**d**	2-O_2N-C_6H_4	93	60	–
5	**e**	4-Cl-C_6H_4	92	67	69
6	**f**	4-F-C_6H_4	89	68	76
7	**g**	4-Me-C_6H_4	87	74	83
8	**h**	4-MeO-C_6H_4	94	69	73
9	**i**	2,4-Cl_2-C_6H_3	86	66	71
10	**j**	2,6-Cl_2-C_6H_3	91	70	74
11	**k**	3,4-$(MeO)_2$-C_6H_3	92	71	68

With the objective of broadening the scope of our strategy, in the next stage of the study we investigated similar reactions with substrates **1l–v** generated from the Baylis–Hillman adducts of several heterocyclic aldehydes, including 2-thiophenecarbaldehyde, 2-furancarbaldehyde, substituted 5-, 4- and 3-isoxazolecarbaldehydes and substituted 3-pyrazolecarbaldehyde. Allylamines **2l** and **2m** derived from 2-thiophenecarbaldehyde and 2-furancarbaldehyde, respectively, undergo a similar series of reactions to furnish **4l** and **4m** in good yields (Table 2). Intriguingly, however, when the allylamine **2n** generated from the Baylis–Hillman acetate **1n** derived from 3-phenyl-5-isoxazolecarbaldehyde was treated with cyanamide in the presence of acetic acid followed by treatment with HCl for 5 min, it resulted in a product that during TLC analysis was observed to be a mixture of two compounds. One of the spots, corresponding to the more polar fraction, showed an intense blue fluorescent colour on TLC similar to the ones observed for **4a–l**. As a result of this observation the reaction mixture with HCl was heated further. It was gratifying to note that the reaction



Scheme 1. Reagents and conditions: (i) 2,2-dimethoxyethylamine, MeOH, room temp., 1 h; (ii) (1) NH_2CN, AcOH/H_2O, 90–100 °C, 2 h, (2) HCl (conc.), 90–100 °C, 5 min; (iii) NaOMe, MeOH, room temp., 1 h; (iv) Ac_2O, pyridine, room temp., 3 h; (v) (1) NH_2CN, AcOH/H_2O (1:1, v/v), 90–100 °C, 2 h, (2) HCl (conc.), 90–100 °C, 30 min (one-pot).

was complete in 30 min, furnishing a pure product in 79% yield that showed an intense blue fluorescent spot. A careful spectral analysis identified the isolated product as the required compound **4n**.

Table 2. Yields of compounds **2**–**4** synthesized from heterocyclic aldehydes.

Entry	Compd. no.	R	Yield [%]		
			2	**3**	**4**
1	**l**	2-thienyl	89	61	71
2	**m**	2-furyl	90	68	67
3	**n**	3-phenylisoxazol-5-yl	88	–	79
4	**o**	3-(2-chlorophenyl)isoxazol-5-yl	87	–	76
5	**p**	3-(4-fluorophenyl)isoxazol-5-yl	91	82[a]	80[b]
6	**q**	3-(4-methylphenyl)isoxazol-5-yl	89	79[a]	73[b]
7	**r**[c]	3-(4-benzyloxyphenyl)isoxazol-5-yl	91‘	–	62
8	**s**	3-(2,4-dichlorophenyl)isoxazol-5-yl	94	–	72
9	**t**	5-phenylisoxazol-3-yl	88	–	68
10	**u**	5-methyl-3-phenylisoxazol-4-yl	87	69	73
11	**v**	1,5-diphenyl-1*H*-pyrazol-3-yl	83	–	48

[a] Yield of product obtained after stopping the reaction within 5 min. [b] Yield obtained by one-pot procedure. [c] The benzyloxy group was debenzylated to the hydroxy group during the treatment with acid.

This encouraged us to examine the versatility of the one-pot reaction for other analogues (**2o**–**s**) obtained from several 3-substituted phenyl-5-isoxazolecarbaldehydes. We were pleased to observe that the reactions of these allylamines (**2o**–**s**) with cyanamide furnished the final products **4o**–**s** in 62–80% yields through a two-step operation in one pot. It was observed that during the acid treatment of allylamine **2r**, debenzylation occurred to afford the product **4r** (Table 2, Entry 7). At the same time, to ascertain that the reaction proceeded by the initial formation of the 2-aminoimidazole derivative, for two of the substrates **2p** and **2q** the reaction was terminated within 2 min of HCl treatment. Suitable workup and isolation yielded the products **3p** and **3q**, respectively. This encouraged us to investigate similar reactions of allylamines derived from the acetates of the Baylis–Hillman adducts of substituted 3-isoxazolecarbaldehyde and substituted 4-isoxazolecarbaldehyde. Hence, as representative examples, the allylamines **2t** and **2u** were prepared from the corresponding acetates **1t** and **1u**. Interestingly, the allylamine **2t** upon treatment with cyanamide under acidic conditions furnished the product **4t** in one pot in 68% yield. In contrast, the allylamine **2u** derived from the acetate **1u** exclusively yielded the corresponding 2-aminopyrazole **3u**. Reaction of **3u** with sodium methoxide under reflux, however, provided the desired product **4u** in 73% yield. This demonstrated that the allylamines generated from the heterocyclic aldehydes,[16] which undergo fast Baylis–Hillman reactions, produce the title compounds in one pot. However, this unusual observation cannot be explained at the present time. We recently reported that 1,5-diaryl-substituted 3-pyrazolecarbaldehyde is also a fast-reacting electrophile for the Baylis–Hillman reaction like 3- and 5-isoxazolecarbaldehydes.[17] Therefore, it was expected that the allylamine **2v** derived from the acetate **1v** would also undergo the acid-mediated cascade cyclization to yield the final product in one pot. Hence the reaction of allylamine **2v** with cyanamide in the presence of acetic acid followed by treatment with HCl was performed. As anticipated, this reaction resulted in the formation of **4v** in one pot, albeit in only 48% yield (Table 2, Entry 11). Consequently, we re-examined the reactions of **2l**, **2m** and **2u** by conducting the reactions for a longer period of time (ca. 24 h), but no change in the outcome was observed. The product from **2m** even decomposed upon prolonged heating.

Conclusions

We have disclosed a facile and general strategy for accessing 6-arylmethylimidazo[1,2-*a*]pyrimidin-7-ylamines from allylamines afforded by the Baylis–Hillman acetates. The title compounds were formed by a one-pot procedure from heterocyclic aldehydes, which undergo fast Baylis–Hillman reactions, whereas all other aldehydes reacted by a two-pot procedure. This synthetic methodology for obtaining the imidazo[1,2-*a*]pyrimidine scaffold is attractive as it involves the use of common reagents and simple reaction conditions.

Experimental Section

General: Melting points are uncorrected and were determined in capillary tubes with an apparatus containing silicon oil. IR spectra were recorded by using a Perkin-Elmer Spectrum RX I FTIR spectrometer. ^{1}H and ^{13}C NMR spectra were recorded either with a Bruker DPX-200 FT or Avance DRX-300 spectrometer by using TMS as the internal standard (chemical shifts given in δ). ES-MS and FAB-MS data were recorded with MICROMASS Quadro-II LCMS and JEOL SX/102/DA 6000 spectrometers, respectively. HRMS data were recorded as EI-HRMS data with a JEOL system or as DART-HRMS data (recorded as ES+) with a JEOL-AccuTOF JMS-T100LC mass spectrometer having a DART (direct analysis in real time) source. Elemental analyses were performed with a Carlo Erba 108 or an Elementar Vario EL III microanalyzer.

General Procedure for the Synthesis of Allylamines 2 as Exemplified for 2a: Acetate **1a** (2.00 g, 9.95 mmol) dissolved in methanol (150 mL) was added dropwise to a solution of 2,2-dimethoxyethylamine (aminoacetaldehyde dimethyl acetal) (3.25 mL, 30.02 mmol) in methanol (20 mL), at room temperature with constant stirring. The reaction was allowed to continue for 1 h, after which the solvent was removed under reduced pressure. The crude product obtained in this fashion was purified by column chromatography on silica gel by using hexanes/ethyl acetate (5:1, v/v) to yield the pure product **2a** (2.13 g, 87%) as a yellow oil.

2-{[(2,2-Dimethoxyethyl)amino]methyl}-3-phenylprop-2-enenitrile (2a): IR (neat): $\tilde{\nu}_{max}$ = 2214 (CN), 3355 (NH) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.80 (d, J = 5.4 Hz, 2 H, CH_2), 3.42 (s, 6 H, 2 × OCH_3), 3.62 (d, J = 1.1 Hz, 2 H, CH_2), 4.52 (t, J = 5.4 Hz, 1 H, CH), 7.12 (s, 1 H, =CH), 7.42–7.45 (m, 3 H, ArH), 7.76–7.79 (m, 2 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 49.7, 53.6, 54.1, 103.9, 110.2, 118.4, 128.7, 128.8, 128.9, 130.3, 144.1 ppm. MS (ES+): m/z = 247.0 [M + 1]$^+$. $C_{14}H_{18}N_2O_2$ (246.1368): calcd. C 68.27, H 7.37, N 11.37; found C 68.45, H 7.58, N 11.25.

3-(2-Chlorophenyl)-2-{[(2,2-dimethoxyethyl)amino]methyl}prop-2-enenitrile (2b): Hexanes/ethyl acetate (5:1); yellow oil (2.27 g from 2.00 g). IR (neat): $\tilde{\nu}_{max}$ = 2216 (CN), 3349 (NH) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 2.81 (d, J = 5.3 Hz, 2 H, CH_2), 3.42 (s, 6 H, 2 × OCH_3), 3.65 (d, J = 1.2 Hz, 2 H, CH_2), 4.51 (t, J = 5.4 Hz, 1 H, CH), 7.33–7.36 (m, 2 H, ArH), 7.42–7.48 (m, 2 H, ArH and =CH), 7.96–7.99 (m, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 49.6, 53.2, 54.1, 103.8, 113.8, 117.6, 127.1, 129.2, 129.7, 131.0, 131.8, 134.0, 140.5 ppm. MS (ES+): m/z = 280.9 $[M + 1]^+$, 249.1 $[M - 31]^+$. $C_{14}H_{17}ClN_2O_2$ (280.0979): calcd. C 59.89, H 6.10, N 9.98; found C 59.84, H 6.22, N 10.09.

2-{[(2,2-Dimethoxyethyl)amino]methyl}-3-(2-fluorophenyl)prop-2-enenitrile (2c): Hexanes/ethyl acetate (5:1); yellow oil (2.15 g from 2.00 g); IR (neat): $\tilde{\nu}_{max}$ = 2215 (CN), 3346 (NH) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 2.79 (d, J = 5.3 Hz, 2 H, CH_2), 3.41 (s, 6 H, 2 × OCH_3), 3.63 (s, 2 H, CH_2), 4.49 (t, J = 5.3 Hz, 1 H, CH), 7.10 (t, J = 9.3 Hz, 1 H, ArH), 7.22 (t, J = 7.6 Hz, 1 H, ArH), 7.36–7.43 (m, 2 H, ArH and =CH), 8.11 (t, J = 7.6 Hz, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 49.7, 53.5, 54.1, 103.9, 112.7, 115.5, 115.8, 117.9, 121.4, 121.6, 124.5, 128.4, 131.9, 132.0, 135.6, 135.7, 158.7, 162.1 ppm. MS (ES+): m/z = 264.9 $[M + 1]^+$, 233.1 $[M - 31]^+$. $C_{14}H_{17}FN_2O_2$ (264.1274): calcd. C 63.62, H 6.48, N 10.60; found C 63.39, H 6.66, N 10.71.

2-{[(2,2-Dimethoxyethyl)amino]methyl}-3-(2-nitrophenyl)prop-2-enenitrile (2d): Hexanes/ethyl acetate (5:1); yellow oil (2.04 g from 1.85 g). IR (neat): $\tilde{\nu}_{max}$ = 2221 (CN), 3434 (NH) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 2.86 (d, J = 5.3 Hz, 2 H, CH_2), 3.44 (s, 6 H, 2 × OCH_3), 3.68 (d, J = 1.4 Hz, 2 H, CH_2), 4.51 (t, J = 5.3 Hz, 1 H, CH), 7.58–7.66 (m, 2 H, ArH and =CH), 7.72–7.83 (m, 2 H, ArH), 8.19–8.21 (dd, J_1 = 1.0, J_2 = 8.2 Hz, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 49.8, 52.6, 54.2, 103.9, 115.6, 117.1, 125.1, 129.9, 130.5, 130.9, 134.1, 141.1, 147.2 ppm. MS (ES+): m/z = 292.0 $[M + 1]^+$. $C_{14}H_{17}N_3O_4$ (291.1219): calcd. C 57.72, H 5.88, N 14.42; found C 57.91, H 6.03, N 14.31.

3-(4-Chlorophenyl)-2-{[(2,2-dimethoxyethyl)amino]methyl}prop-2-enenitrile (2e): Hexanes/ethyl acetate (5:1); yellow oil (2.30 g from 2.00 g). IR (neat): $\tilde{\nu}_{max}$ = 2213 (CN), 3429 (NH) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 2.78 (d, J = 5.3 Hz, 2 H, CH_2), 3.41 (s, 6 H, 2 × OCH_3), 3.60 (d, J = 1.0 Hz, 2 H, CH_2), 4.49 (t, J = 5.3 Hz, 1 H, CH), 7.07 (s, 1 H, =CH), 7.39 (d, J = 8.6 Hz, 2 H, ArH), 7.70 (d, J = 8.6 Hz, 2 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 49.7, 53.5, 54.1, 103.8, 111.0, 118.1, 129.1, 130.0, 131.7, 136.1, 142.4 ppm. MS (ES+): m/z = 280.9 $[M + 1]^+$, 249.1 $[M - 31]^+$. $C_{14}H_{17}ClN_2O_2$ (280.0979): calcd. C 59.89, H 6.10, N 9.98; found C 59.62, H 6.41, N 9.76.

2-{[(2,2-Dimethoxyethyl)amino]methyl}-3-(4-fluorophenyl)prop-2-enenitrile (2f): Hexanes/ethyl acetate (5:1); yellow oil (2.15 g from 2.00 g). IR (neat): $\tilde{\nu}_{max}$ = 2213 (CN), 3346 (NH) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 2.78 (d, J = 5.4 Hz, 2 H, CH_2), 3.41 (s, 6 H, 2 × OCH_3), 3.60 (s, 2 H, CH_2), 4.49 (t, J = 5.3 Hz, 1 H, CH), 7.08–7.14 (m, 3 H, ArH and =CH), 7.75–7.79 (m, 2 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 49.7, 53.5, 54.1, 103.8, 110.0, 115.8, 116.1, 118.2, 129.5, 130.8, 130.9, 142.6, 161.9, 165.2 ppm. MS (ES+): m/z = 264.9 $[M + 1]^+$. $C_{14}H_{17}FN_2O_2$ (264.1274): calcd. C 63.62, H 6.48, N 10.60; found C 63.56, H 6.75, N 10.46.

2-{[(2,2-Dimethoxyethyl)amino]methyl}-3-(4-methylphenyl)prop-2-enenitrile (2g): Hexanes/ethyl acetate (5:1); yellow oil (2.42 g from 2.30 g). IR (neat): $\tilde{\nu}_{max}$ = 2212 (CN), 3432 (NH) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 2.38 (s, 3 H, CH_3), 2.77 (d, J = 5.3 Hz, 2 H, CH_2), 3.40 (s, 6 H, 2 × OCH_3), 3.58 (s, 2 H, CH_2), 4.49 (t, J = 5.4 Hz, 1 H, CH), 7.05 (s, 1 H, =CH), 7.22 (d, J = 8.0 Hz, 2 H, ArH), 7.66 (d, J = 8.1 Hz, 2 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.5, 49.7, 53.7, 54.1, 103.9, 108.9, 118.6, 128.9, 129.6, 130.6, 140.8, 144.1 ppm. MS (ES+): m/z = 260.9 $[M + 1]^+$, 229.0 $[M - 31]^+$. $C_{15}H_{20}N_2O_2$ (260.1525): calcd. C 69.20, H 7.74, N 10.76; found C 68.97, H 8.06, N 10.53.

2-{[(2,2-Dimethoxyethyl)amino]methyl}-3-(4-methoxyphenyl)prop-2-enenitrile (2h): Hexanes/ethyl acetate (4:1); yellow oil (2.13 g from 1.90 g). IR (neat): $\tilde{\nu}_{max}$ = 2209 (CN), 3434 (NH) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 2.77 (d, J = 5.4 Hz, 2 H, CH_2), 3.40 (s, 6 H, 2 × OCH_3), 3.56 (d, J = 0.7 Hz, 2 H, CH_2), 3.84 (s, 3 H, OCH_3), 4.49 (t, J = 5.4 Hz, 1 H, CH), 6.93 (d, J = 8.9 Hz, 2 H, ArH), 7.01 (s, 1 H, =CH), 7.74 (d, J = 8.8 Hz, 2 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 49.6, 53.7, 54.0, 55.3, 103.8, 107.0, 114.2, 118.9, 126.0, 130.6, 143.7, 161.1 ppm. MS (ES+): m/z = 276.9 $[M + 1]^+$, 245.0 $[M - 31]^+$. $C_{15}H_{20}N_2O_3$ (276.1474): calcd. C 65.20, H 7.30, N 10.14; found C 65.01, H 7.67, N 10.25.

3-(2,4-Dichlorophenyl)-2-{[(2,2-dimethoxyethyl)amino]methyl}prop-2-enenitrile (2i): Hexanes/ethyl acetate (7:1); yellow oil (2.01 g from 2.00 g). IR (neat): $\tilde{\nu}_{max}$ = 2217 (CN), 3432 (NH) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 2.80 (d, J = 5.3 Hz, 2 H, CH_2), 3.42 (s, 6 H, 2 × OCH_3), 3.64 (s, 2 H, CH_2), 4.50 (t, J = 5.3 Hz, 1 H, CH), 7.29–7.35 (m, 1 H, ArH), 7.41 (s, 1 H, =CH), 7.46 (d, J = 1.7 Hz, 1 H, ArH), 7.93 (d, J = 8.4 Hz, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 49.6, 53.1, 54.0, 54.1, 103.8, 114.4, 117.4, 127.5, 129.6, 129.8, 134.7, 136.3, 139.1, 141.5 ppm. MS (ES+): m/z = 314.9 $[M + 1]^+$, 283.1 $[M - 31]^+$. $C_{14}H_{16}Cl_2N_2O_2$ (314.0589): calcd. C 53.35, H 5.12, N 8.89; found C 53.26, H 5.38, N 8.68.

3-(2,6-Dichlorophenyl)-2-{[(2,2-dimethoxyethyl)amino]methyl}prop-2-enenitrile (2j): Hexanes/ethyl acetate (7:1); yellow oil (2.23 g from 2.10 g). IR (neat): $\tilde{\nu}_{max}$ = 2223 (CN), 3432 (NH) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 2.84 (d, J = 5.3 Hz, 2 H, CH_2), 3.41 (s, 6 H, 2 × OCH_3), 3.67 (d, J = 1.2 Hz, 2 H, CH_2), 4.50 (t, J = 5.3 Hz, 1 H, CH), 7.11 (s, 1 H, =CH), 7.25–7.28 (m, 1 H, ArH), 7.38 (d, J = 8.2 Hz, 2 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 49.4, 52.1, 54.0, 103.8, 116.3, 120.5, 128.2, 130.3, 132.1, 134.2, 139.0 ppm. MS (ES+): m/z = 314.9 $[M + 1]^+$, 283.1 $[M - 31]^+$. $C_{14}H_{16}Cl_2N_2O_2$ (314.0589): calcd. C 53.35, H 5.12, N 8.89; found C 53.48, H 5.23, N 8.74.

2-{[(2,2-Dimethoxyethyl)amino]methyl}-3-(3,4-dimethoxyphenyl)-prop-2-enenitrile (2k): Hexanes/ethyl acetate (4:1); a white solid (2.16 g from 2.00 g), m.p. 80–81 °C. IR (KBr): $\tilde{\nu}_{max}$ = 2210 (CN), 3370 (NH) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 2.78 (d, J = 5.3 Hz, 2 H, CH_2), 3.40 (s, 6 H, 2 × OCH_3), 3.58 (s, 2 H, CH_2), 3.92 (s, 3 H, OCH_3), 3.93 (s, 3 H, OCH_3), 4.49 (t, J = 5.3 Hz, 1 H, CH), 6.88 (d, J = 8.3 Hz, 1 H, ArH), 7.01 (s, 1 H, =CH), 7.21–7.23 (dd, J_1 = 1.8, J_2 = 8.3 Hz, 1 H, ArH), 7.57 (d, J = 1.7 Hz, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 49.6, 53.7, 54.1, 54.3, 55.9, 103.8, 107.1, 110.5, 110.8, 119.0, 123.5, 126.2, 144.0, 149.0, 150.9 ppm. MS (ES+): m/z = 306.9 $[M + 1]^+$. $C_{16}H_{22}N_2O_4$ (306.1580): calcd. C 62.73, H 7.24, N 9.14; found C 62.59, H 7.48, N 9.35.

2-{[(2,2-Dimethoxyethyl)amino]methyl}-3-(2-thienyl)prop-2-enenitrile (2l): Hexanes/ethyl acetate (5:1); yellow oil (2.34 g from 2.16 g); IR (neat): $\tilde{\nu}_{max}$ = 2208 (CN), 3346 (NH) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 2.77 (d, J = 5.3 Hz, 2 H, CH_2), 3.40 (s, 6 H, 2 × OCH_3), 3.57 (d, J = 0.57 Hz, 2 H, CH_2), 4.48 (t, J = 5.3 Hz, 1 H, CH), 7.08–7.11 (m, 1 H, ArH), 7.23 (s, 1 H, =CH), 7.47 (d, J = 5.0 Hz, 1 H, ArH), 7.51 (d, J = 3.5 Hz, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 49.7, 52.8, 54.1, 103.8, 107.1, 118.5, 127.5, 129.2, 131.3, 136.4, 137.2 ppm. MS (ES+): m/z = 253.3 $[M + 1]^+$. $C_{12}H_{16}N_2O_2S$ (252.0932): calcd. C 57.12, H 6.39, N 11.10; found C 57.35, H 6.12, N 10.96.

2-{[(2,2-Dimethoxyethyl)amino]methyl}-3-(2-furyl)prop-2-enenitrile (2m): Hexanes/ethyl acetate (4:1); yellow oil (2.50 g from 2.25 g). IR (neat): $\tilde{\nu}_{max}$ = 2212 (CN), 3404 (NH) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 2.78 (d, J = 5.3 Hz, 2 H, CH_2), 3.42 (s, 6 H, 2 × OCH_3), 3.57 (d, J = 0.9 Hz, 2 H, CH_2), 4.50 (t, J = 5.4 Hz, 1 H, CH), 6.52–6.54 (m, 1 H, ArH), 6.97–7.04 (m, 2 H, ArH and =CH), 7.55 (d, J = 1.4 Hz, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 49.4, 52.4, 54.2, 103.6, 103.6, 105.9, 112.3, 114.4, 118.2, 131.3, 144.5, 149.4 ppm. MS (ES+): m/z = 237.0 $[M + 1]^+$. $C_{12}H_{16}N_2O_3$ (236.1161): calcd. C 61.00, H 6.83, N 11.86; found C 61.19, H 6.98, N 11.76.

2-{[(2,2-Dimethoxyethyl)amino]methyl}-3-(3-phenylisoxazol-5-yl)-prop-2-enenitrile (2n): Hexanes/ethyl acetate (3:1); a white solid (2.23 g from 2.16 g), m.p. 86–88 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1628 (C=N), 2220 (CN), 3432 (NH) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 2.80 (d, J = 5.2 Hz, 2 H, CH_2), 3.42 (s, 6 H, 2 × OCH_3), 3.66 (d, J = 1.5 Hz, 2 H, CH_2), 4.49 (t, J = 5.2 Hz, 1 H, CH), 7.27 (s, 1 H, =CH), 7.33 (s, 1 H, ArH), 7.47–7.50 (m, 3 H, ArH), 7.84–7.88 (m, 2 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 50.1, 52.4, 54.3, 103.0, 103.9, 116.4, 116.8, 126.9, 127.7, 128.4, 129.1, 130.4, 163.1, 165.1 ppm. MS (ES+): m/z = 314.0 $[M + 1]^+$. $C_{17}H_{19}N_3O_3$ (313.1426): calcd. C 65.16, H 6.11, N 13.41; found C 65.37, H 6.44, N 13.28.

3-[3-(2-Chlorophenyl)isoxazol-5-yl]-2-{[(2,2-dimethoxyethyl)-amino]methyl}prop-2-enenitrile (2o): Hexanes/ethyl acetate (3:1); yellow oil (2.10 g from 2.10 g). IR (neat): $\tilde{\nu}_{max}$ = 1645 (C=N), 2218 (CN), 3349 (NH) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 2.81 (d, J = 5.3 Hz, 2 H, CH_2), 3.43 (s, 6 H, 2 × OCH_3), 3.68 (d, J = 1.4 Hz, 2 H, CH_2), 4.50 (t, J = 5.2 Hz, 1 H, CH), 7.30 (s, 1 H, =CH), 7.39–7.48 (m, 3 H, ArH), 7.52–7.55 (m, 1 H, ArH), 7.74–7.78 (m, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 50.4, 52.8, 54.6, 54.7, 104.3, 106.8, 116.9, 127.6, 127.9, 130.9, 131.4, 131.6, 133.4, 162.1, 164.8 ppm. MS (ES+): m/z = 347.8 $[M + 1]^+$, 316.0 $[M - 31]^+$. $C_{17}H_{18}ClN_3O_3$ (347.1037): calcd. C 58.71, H 5.22, N 12.08; found C 58.88, H 5.29, N 12.26.

2-{[(2,2-Dimethoxyethyl)amino]methyl}-3-[3-(4-fluorophenyl)isoxazol-5-yl]prop-2-enenitrile (2p): Hexanes/ethyl acetate (3:1); a white solid (2.05 g from 1.95 g), m.p. 101–103 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1609 (C=N), 2219 (CN), 3385 (NH) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 2.79 (d, J = 5.3 Hz, 2 H, CH_2), 3.42 (s, 6 H, 2 × OCH_3), 3.67 (d, J = 1.4 Hz, 2 H, CH_2), 4.48 (t, J = 5.2 Hz, 1 H, CH), 7.14–7.20 (m, 2 H, ArH), 7.28 (s, 1 H, =CH), 7.29 (s, 1 H, ArH), 7.82–7.86 (m, 2 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 50.0, 52.3, 54.3, 102.7, 103.8, 116.0, 116.3, 116.5, 116.8, 124.5, 124.6, 127.6, 128.8, 128.9, 162.1, 165.2 ppm. MS (ES+): m/z = 331.8 $[M + 1]^+$, 300.1 $[M - 31]^+$. $C_{17}H_{18}FN_3O_3$ (331.1332): calcd. C 61.62, H 5.48, N 12.68; found C 61.89, H 5.65, N 12.51.

2-{[(2,2-Dimethoxyethyl)amino]methyl}-3-[3-(4-methylphenyl)isoxazol-5-yl]prop-2-enenitrile (2q): Hexanes/ethyl acetate (5:2); yellow oil (2.04 g from 1.98 g). IR (neat): $\tilde{\nu}_{max}$ = 1616 (C=N), 2220 (CN), 3368 (NH) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 2.43 (s, 3 H, CH_3), 2.81 (d, J = 5.2 Hz, 2 H, CH_2), 3.43 (s, 6 H, 2 × OCH_3), 3.67 (d, J = 1.1 Hz, 2 H, CH_2), 4.50 (t, J = 5.2 Hz, 1 H, CH), 7.28–7.33 (m, 4 H, ArH and =CH), 7.76 (d, J = 8.1 Hz, 2 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 21.9, 50.4, 52.7, 54.7, 103.3, 104.2, 116.5, 117.3, 125.9, 127.2, 128.2, 130.2, 141.0, 163.4, 165.2 ppm. MS (ES+): m/z = 328.1 $[M + 1]^+$, 297.3 $[M - 31]^+$. $C_{18}H_{21}N_3O_3$ (327.1583): calcd. C 66.04, H 6.47, N 12.84; found C 66.17, H 6.69, N 12.96.

3-[3-(4-Benzyloxyphenyl)isoxazol-5-yl]-2-{[(2,2-dimethoxyethyl)-amino]methyl}prop-2-enenitrile (2r): Hexanes/ethyl acetate (7:3); a white solid (2.35 g from 2.31 g), m.p. 88–90 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1628 (C=N), 2220 (CN), 3432 (NH) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 2.80 (d, J = 5.3 Hz, 2 H, CH_2), 3.43 (s, 6 H, 2 × OCH_3), 3.66 (d, J = 0.8 Hz, 2 H, CH_2), 4.50 (t, J = 5.2 Hz, 1 H, CH), 5.13 (s, 2 H, CH_2), 7.08 (d, J = 8.7 Hz, 2 H, ArH), 7.25 (s, 1 H, =CH), 7.28 (s, 1 H, ArH), 7.36–7.48 (m, 5 H, ArH), 7.80 (d, J = 8.7 Hz, 2 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 49.9, 52.2, 54.2, 70.0, 102.7, 103.8, 113.9, 115.2, 116.0, 116.8, 121.0, 127.0, 127.4, 128.1, 128.3, 128.6, 136.4, 160.4, 162.6, 164.7 ppm. MS (ES+): m/z = 420.0 $[M + 1]^+$. $C_{24}H_{25}N_3O_4$ (419.1845): calcd. C 68.72, H 6.01, N 10.02; found C 68.98, H 6.37, N 9.87.

3-[3-(2,4-Dichlorophenyl)isoxazol-5-yl]-2-{[(2,2-dimethoxyethyl)-amino]methyl}prop-2-enenitrile (2s): Hexanes/ethyl acetate (3:1); yellow oil (2.24 g from 2.10 g). IR (neat): $\tilde{\nu}_{max}$ = 1649 (C=N), 2220 (CN), 3415 (NH) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 2.79 (d, J = 5.2 Hz, 2 H, CH_2), 3.42 (s, 6 H, 2 × OCH_3), 3.67 (d, J = 1.2 Hz, 2 H, CH_2), 4.48 (t, J = 5.2 Hz, 1 H, CH), 7.29 (d, J = 1.9 Hz, 1 H, ArH), 7.36–7.38 (dd, J_1 = 2.0, J_2 = 8.4 Hz, 1 H, ArH), 7.45 (s, 1 H, =CH), 7.54 (d, J = 2.0 Hz, 1 H, ArH), 7.71 (d, J = 8.4 Hz, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 50.0, 52.3, 54.3, 103.8, 106.1, 116.6, 116.8, 126.2, 127.3, 127.6, 130.4, 131.7, 133.7, 136.7, 160.8, 164.6 ppm. MS (ES+): m/z = 381.9 $[M + 1]^+$, 350.4 $[M - 31]^+$. $C_{17}H_{17}Cl_2N_3O_3$ (381.0647): calcd. C 53.42, H 4.48, N 10.99; found C 53.53, H 4.80, N 11.06.

2-{[(2,2-Dimethoxyethyl)amino]methyl}-3-(5-phenylisoxazol-3-yl)-prop-2-enenitrile (2t): Hexanes/ethyl acetate (3:1); a white solid (2.06 g from 2.00 g), m.p. 85–87 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1616 (C=N), 2211 (CN), 3416 (NH) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 2.80 (d, J = 5.3 Hz, 2 H, CH_2), 3.42 (s, 6 H, 2 × OCH_3), 3.67 (d, J = 1.0 Hz, 2 H, CH_2), 4.50 (t, J = 5.3 Hz, 1 H, CH), 7.34 (s, 1 H, =CH), 7.35 (s, 1 H, ArH), 7.48–7.51 (m, 3 H, ArH), 7.83–7.86 (m, 2 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 49.9, 52.8, 54.3, 97.6, 103.8, 117.1, 117.6, 126.0, 126.8, 129.1, 130.7, 131.5, 158.7, 171.1 ppm. MS (ES+): m/z = 313.8 $[M + 1]^+$, 282.1 $[M - 31]^+$. $C_{17}H_{19}N_3O_3$ (313.1426): calcd. C 65.16, H 6.11, N 13.41; found C 65.29, H 6.01, N 13.58.

2-{[(2,2-Dimethoxyethyl)amino]methyl}-3-(5-methyl-3-phenylisoxazol-4-yl)prop-2-enenitrile (2u): Hexanes/ethyl acetate (3:1); colourless oil (2.22 g from 2.20 g). IR (neat): $\tilde{\nu}_{max}$ = 1638 (C=N), 2218 (CN), 3354 (NH) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 2.57 (s, 3 H, CH_3), 2.78 (d, J = 5.3 Hz, 2 H, CH_2), 3.40 (s, 6 H, 2 × OCH_3), 3.62 (d, J = 0.9 Hz, 2 H, CH_2), 4.47 (t, J = 5.3 Hz, 1 H, CH), 6.93 (s, 1 H, =CH), 7.47–7.49 (m, 3 H, ArH), 7.58–7.62 (m, 2 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.8, 49.8, 52.4, 54.2, 103.8, 110.1, 117.1, 117.4, 128.2, 128.5, 129.0, 130.1, 133.7, 161.3, 168.5 ppm. MS (ES+): m/z = 327.9 $[M + 1]^+$, 296.0 $[M - 31]^+$. $C_{18}H_{21}N_3O_3$ (327.1583): calcd. C 66.04, H 6.47, N 12.84; found C 66.10, H 6.78, N 12.78.

2-{[(2,2-Dimethoxyethyl)amino]methyl}-3-(1,5-diphenyl-1*H*-pyrazol-3-yl)prop-2-enenitrile (2v): Hexanes/ethyl acetate (5:3); yellow oil (2.16 g from 2.30 g). IR (neat): $\tilde{\nu}_{max}$ = 1636 (C=N), 2213 (CN), 3425 (NH) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 2.80 (d, J = 5.4 Hz, 2 H, CH_2), 3.41 (s, 6 H, 2 × OCH_3), 3.64 (s, 2 H, CH_2), 4.51 (t, J = 5.4 Hz, 1 H, CH), 7.24–7.38 (m, 12 H, ArH and =CH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 49.6, 53.0, 54.1, 103.8, 107.2, 110.8, 118.3, 125.2, 128.1, 128.6, 128.8, 129.1, 129.7, 136.7, 139.5, 144.7, 147.1 ppm. MS (ES+): m/z = 389.1 $[M + 1]^+$, 357.2 $[M - 31]^+$. $C_{23}H_{24}N_4O_2$ (388.1899): calcd. C 71.11, H 6.23, N 14.42; found C 71.32, H 6.42, N 14.32.

General Procedure for the Synthesis of Substituted 2-Aminoimidazoles 3 as Exemplified for 3a: Cyanamide (0.52 g, 12.38 mmol) was added to the allylamine **2a** (1.50 g, 6.10 mmol) dissolved in aqueous acetic acid (0.36 mL in 1 mL of H_2O), and the reaction mixture

was heated at 100 °C for 2 h. Thereafter, conc. HCl (5 mL) was added to the reaction mixture, and it was further heated for 5 min. Then the reaction mixture was diluted with water (50 mL), neutralized with $NaHCO_3$ and extracted with ethyl acetate (4 × 20 mL). The organic layers were combined, dried with Na_2SO_4, concentrated, and the residue thus obtained was purified by silica gel column chromatography. Elution with ethyl acetate/methanol (19:1, v/v) gave the pure product **3a** in 72% yield (0.98 g).

2-[(2-Amino-1*H*-imidazol-1-yl)methyl]-3-phenylprop-2-enenitrile (3a): White solid, m.p. 163–165 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1639 (C=N), 2214 (CN), 3407 (NH_2) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 4.25 (br. s, 2 H, NH_2), 4.67 (s, 2 H, CH_2), 6.64 (s, 1 H, ArH), 6.74 (s, 1 H, ArH), 6.92 (s, 1 H, =CH), 7.44–7.45 (m, 3 H, ArH), 7.73–7.76 (m, 2 H, ArH) ppm. ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ = 47.7, 108.1, 115.1, 118.2, 124.8, 129.4, 129.8, 131.5, 133.6, 145.7, 150.0 ppm. MS (ES+): *m*/*z* = 225.1 [M + 1]$^+$. HRMS (EI): calcd. for $C_{13}H_{12}N_4$ 224.1062; found 224.1055.

2-[(2-Amino-1*H*-imidazol-1-yl)methyl]-3-(2-chlorophenyl)prop-2-enenitrile (3b): Ethyl acetate/methanol (20:1); white solid (1.02 g from 1.60 g), m.p. 227–230 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1659 (C=N), 2215 (CN), 3428 (NH_2) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 300 MHz): δ = 5.04 (d, *J* = 2.2 Hz, 2 H, CH_2), 6.67 (d, *J* = 1.1 Hz, 1 H, ArH), 6.89 (d, *J* = 1.1 Hz, 1 H, ArH), 7.45–7.48 (m, 3 H, ArH and =CH), 7.58–7.61 (m, 1 H, ArH), 7.84 (s, 1 H, ArH) ppm. ^{13}C NMR ([D$_6$]-DMSO, 75 MHz): δ = 43.7, 116.3, 125.9, 126.4, 127.9, 130.0, 131.5, 132.6, 134.0, 134.4, 141.4, 164.8 ppm. MS (ES+): *m*/*z* = 259.2 [M + 1]$^+$. HRMS (EI): calcd. for $C_{13}H_{11}ClN_4$ 258.0672; found 258.0679.

2-[(2-Amino-1*H*-imidazol-1-yl)methyl]-3-(2-fluorophenyl)prop-2-enenitrile (3c): Ethyl acetate/methanol (20:1); white solid (0.95 g from 1.55 g), m.p. 158–160 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1620 (C=N), 2214 (CN), 3415 (NH_2) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 300 MHz): δ = 4.82 (s, 2 H, CH_2), 5.57 (s, 2 H, NH_2, replaceable by D_2O), 6.45 (d, *J* = 1.4 Hz, 1 H, ArH), 6.65 (d, *J* = 1.4 Hz, 1 H, ArH), 7.30–7.36 (m, 3 H, ArH and =CH), 7.52–7.55 (m, 1 H, ArH), 7.88–7.95 (m, 1 H, ArH) ppm. ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ = 47.3, 100.2, 111.4, 111.5, 114.9, 116.5, 116.8, 117.5, 121.4, 121.6, 124.9, 125.5, 125.6, 128.9, 128.9, 133.4, 133.5, 136.9, 137.0, 149.9, 158.7, 162.0 ppm. MS (ES+): *m*/*z* = 243.4 [M + 1]$^+$. HRMS (EI): calcd. for $C_{13}H_{11}FN_4$ 242.0968; found 242.0965.

2-[(2-Amino-1*H*-imidazol-1-yl)methyl]-3-(2-nitrophenyl)prop-2-enenitrile (3d): Ethyl acetate/methanol (20:1); white solid (0.95 g from 1.72 g), m.p. 133–136 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1638 (C=N), 2224 (CN), 3446 (NH_2) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 300 MHz): δ = 4.83 (d, *J* = 1.0 Hz, 2 H, CH_2), 5.63 (s, 2 H, NH_2), 6.48 (d, *J* = 1.6 Hz, 1 H, ArH), 6.66 (d, *J* = 1.6 Hz, 1 H, ArH), 7.65 (s, 1 H, =CH), 7.72–7.78 (m, 2 H, ArH), 7.87–7.93 (m, 1 H, ArH), 8.21–8.23 (m, 1 H, ArH) ppm. ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ = 46.7, 112.6, 114.8, 116.9, 123.7, 125.7, 129.7, 131.4, 131.8, 135.2, 143.7, 147.6, 149.8 ppm. MS (ES+): *m*/*z* = 270.2 [M + 1]$^+$. HRMS (EI): calcd. for $C_{13}H_{11}N_5O_2$ 269.0913; found 269.0936.

2-[(2-Amino-1*H*-imidazol-1-yl)methyl]-3-(4-chlorophenyl)prop-2-enenitrile (3e): Ethyl acetate/methanol (20:1); white solid (1.01 g from 1.63 g), m.p. 120–122 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1635 (C=N), 2215 (CN), 3431 (NH_2) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 300 MHz): δ = 4.77 (s, 2 H, CH_2), 5.65 (br. s, 2 H, NH_2), 6.46 (s, 1 H, ArH), 6.65 (s, 1 H, ArH), 7.33 (s, 1 H, =CH), 7.54–7.59 (m, 2 H, ArH), 7.74 (d, *J* = 6.5 Hz, 2 H, ArH) ppm. ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ = 47.4, 108.8, 114.9, 117.8, 124.4, 129.6, 129.8, 130.8, 131.0, 132.3, 135.8, 144.2, 149.2 ppm. MS (ES+): *m*/*z* = 259.1 [M + 1]$^+$. $C_{13}H_{11}ClN_4$ (258.0672): calcd. C 60.35, H 4.29, N 21.66; found C 60.58, H 4.62, N 21.43.

2-[(2-Amino-1*H*-imidazol-1-yl)methyl]-3-(4-fluorophenyl)prop-2-enenitrile (3f): Ethyl acetate/methanol (19:1); white solid (0.98 g from 1.57 g), m.p. 234–236 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1663 (C=N), 2213 (CN), 3452 (NH_2) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 300 MHz): δ = 5.10 (s, 2 H, CH_2), 7.00 (d, *J* = 2.4 Hz, 1 H, ArH), 7.09 (d, *J* = 2.4 Hz, 1 H, ArH), 7.34–7.40 (m, 2 H, ArH), 7.78 (s, 1 H, =CH), 7.81–7.85 (m, 2 H, ArH), 8.14 (s, 2 H, NH_2, exchangeable by D_2O) ppm. ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ = 47.7, 105.0, 113.9, 116.6, 116.8, 117.3, 129.6, 131.7, 131.9, 146.4, 147.1, 162.1, 165.4 ppm. MS (ES+): *m*/*z* = 243.4 [M + 1]$^+$. HRMS (EI): calcd. for $C_{13}H_{11}FN_4$ 242.0968; found 242.0955.

2-[(2-Amino-1*H*-imidazol-1-yl)methyl]-3-(4-methylphenyl)prop-2-enenitrile (3g): Ethyl acetate/methanol (20:1); white solid (0.99 g from 1.47 g), m.p. 221–224 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1661 (C=N), 2207 (CN), 3243 (NH_2) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 300 MHz): δ = 2.35 (s, 3 H, CH_3), 5.09 (s, 2 H, CH_2), 6.99 (d, *J* = 2.3 Hz, 1 H, ArH), 7.08 (d, *J* = 2.4 Hz, 1 H, ArH), 7.31 (d, *J* = 4.4 Hz, 2 H, ArH), 7.67 (d, *J* = 8.1 Hz, 2 H, ArH), 7.72 (s, 1 H, =CH), 8.14 (s, 2 H, NH_2) ppm. ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ = 21.7, 47.9, 104.1, 114.0, 116.7, 117.7, 129.4, 130.2, 130.4, 141.9, 147.2, 147.7 ppm. MS (ES+): *m*/*z* = 239.1 [M + 1]$^+$. HRMS (EI): calcd. for $C_{14}H_{14}N_4$ 238.1218; found 238.1207.

2-[(2-Amino-1*H*-imidazol-1-yl)methyl]-3-(4-methoxyphenyl)prop-2-enenitrile (3h): Ethyl acetate/methanol (17:1); white solid (0.95 g from 1.50 g), m.p. 205–207 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1663 (C=N), 2217 (CN), 3245 (NH_2) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 300 MHz): δ = 3.81 (s, 3 H, OCH_3), 5.05 (s, 2 H, CH_2), 6.99 (d, *J* = 2.4 Hz, 1 H, ArH), 7.06–7.09 (m, 3 H, ArH and =CH), 7.69 (m, 1 H, ArH), 7.76 (d, *J* = 8.8 Hz, 2 H, ArH), 8.11 (s, 2 H, NH_2) ppm. ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ = 47.9, 56.0, 101.8, 113.9, 115.1, 116.6, 118.0, 125.6, 131.3, 147.1, 147.4, 162.0 ppm. MS (ES+): *m*/*z* = 255.0 [M + 1]$^+$. $C_{14}H_{14}N_4O$ (254.1168): calcd. C 66.13, H 5.55, N 22.03; found C 65.89, H 5.83, N 22.21.

2-[(2-Amino-1*H*-imidazol-1-yl)methyl]-3-(2,4-dichlorophenyl)prop-2-enenitrile (3i): Ethyl acetate/methanol (22:1); white solid (1.01 g from 1.65 g), m.p. 238–241 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1645 (C=N), 2219 (CN), 3432 (NH_2) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 300 MHz): δ = 5.15 (s, 2 H, CH_2), 7.01 (d, *J* = 1.7 Hz, 1 H, ArH), 7.07 (d, *J* = 1.9 Hz, 1 H, ArH), 7.58–7.61 (dd, J_1 = 1.6, J_2 = 8.4 Hz, 1 H, ArH), 7.72 (s, 1 H, =CH), 7.79 (d, *J* = 1.7 Hz, 1 H, ArH), 7.85 (d, *J* = 8.4 Hz, 1 H, ArH), 8.12 (s, 2 H, NH_2) ppm. ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ = 47.2, 110.7, 114.0, 116.4, 116.7, 128.5, 130.0, 130.7, 131.0, 134.6, 136.4, 142.7, 147.2 ppm. MS (ES+): *m*/*z* = 293.2 [M + 1]$^+$. $C_{13}H_{10}Cl_2N_4$ (292.0283): calcd. C 53.26, H 3.44, N 19.11; found C 53.12, H 24.38, N 18.98.

2-[(2-Amino-1*H*-imidazol-1-yl)methyl]-3-(2,6-dichlorophenyl)prop-2-enenitrile (3j): Ethyl acetate/methanol (18:1); white solid (1.12 g from 1.72 g), m.p. 268–270 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1663 (C=N), 2224 (CN), 3246 (NH_2) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 300 MHz): δ = 5.17 (s, 2 H, CH_2), 6.80 (s, 1 H, ArH), 6.90 (s, 1 H, ArH), 7.32–7.42 (m, 3 H, ArH and =CH), 7.63 (s, 1 H, ArH), 8.06 (s, 2 H, NH_2) ppm. ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ = 47.1, 114.8, 116.1, 116.2, 117.2, 129.9, 132.1, 133.1, 134.2, 144.6, 147.7 ppm. MS (ES+): *m*/*z* = 293.2 [M + 1]$^+$. HRMS (EI): calcd. for $C_{13}H_{10}Cl_2N_4$ 292.0283; found 292.0283.

2-[(2-Amino-1*H*-imidazol-1-yl)methyl]-3-(3,4-dimethoxyphenyl)-prop-2-enenitrile (3k): Ethyl acetate/methanol (17:1); white solid (1.05 g from 1.60 g), m.p. 252–255 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1663 (C=N), 2217 (CN), 3245 (NH_2) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 300 MHz): δ = 3.83 (s, 6 H, 2 × OCH_3), 5.18 (d, *J* = 2.2 Hz, 2 H, CH_2), 6.67 (d, *J* = 1.2 Hz, 1 H, ArH), 6.94 (d, *J* = 1.3 Hz, 1 H, ArH), 7.08 (s, 2 H, ArH), 7.11 (s, 1 H, =CH), 7.76 (s, 1 H, ArH)

ppm. ^{13}C NMR ([D$_6$]DMSO, 50 MHz): δ = 47.9, 56.3, 56.5, 103.8, 112.0, 112.6, 115.7, 118.8, 120.2, 124.1, 126.2, 146.7, 149.5, 152.0, 167.2 ppm. MS (ES+): *m*/*z* = 285.1 [M + 1]$^+$. HRMS (EI): calcd. for $C_{15}H_{16}N_4O_2$ 284.1273; found 284.1277.

2-[(2-Amino-1*H*-imidazol-1-yl)methyl]-3-(2-thienyl)prop-2-enenitrile (3l): Ethyl acetate/methanol (19:1); white solid (0.92 g from 1.65 g), m.p. 193–195 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1643 (C=N), 2212 (CN), 3406 (NH$_2$) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 5.13 (d, *J* = 2.3 Hz, 2 H, CH$_2$), 6.71 (d, *J* = 1.4 Hz, 1 H, ArH), 7.02 (d, *J* = 1.4 Hz, 1 H, ArH), 7.29–7.32 (m, 1 H, ArH), 7.60 (d, *J* = 3.5 Hz, 1 H, =CH), 7.97–8.01 (m, 2 H, ArH) ppm. ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ = 43.4, 115.0, 118.2, 124.7, 127.8, 128.8, 131.2, 132.6, 136.3, 140.0, 160.0 ppm. MS (ES+): *m*/*z* = 231.3 [M + 1]$^+$. HRMS (EI): calcd. for $C_{11}H_{10}N_4S$ 230.0626; found 230.0625.

2-[(2-Amino-1*H*-imidazol-1-yl)methyl]-3-(2-furyl)prop-2-enenitrile (3m): Ethyl acetate/methanol (19:1); white solid (0.94 g from 1.53 g), m.p. 159–160 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1643 (C=N), 2212 (CN), 3406 (NH$_2$) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 4.70 (s, 2 H, CH$_2$), 5.47 (s, 2 H, NH$_2$), 6.42 (d, *J* = 1.4 Hz, 1 H, ArH), 6.61 (d, *J* = 1.5 Hz, 1 H, ArH), 6.68–6.70 (m, 1 H, ArH), 7.02 (d, *J* = 3.5 Hz, 1 H, ArH), 7.05 (m, 1 H, =CH), 7.92 (d, *J* = 1.3 Hz, 1 H, ArH) ppm. ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ = 46.8, 103.9, 113.5, 114.9, 116.6, 118.05, 124.8, 131.8, 146.7, 149.2, 149.8 ppm. MS (ES+): *m*/*z* = 215.1 [M + 1]$^+$. HRMS (EI): calcd. for $C_{11}H_{10}N_4O$ 214.0855; found 214.0847.

2-[(2-Amino-1*H*-imidazol-1-yl)methyl]-3-[3-(4-fluorophenyl)-isoxazol-5-yl]prop-2-enenitrile (3p): Ethyl acetate/methanol (18:1); white solid (1.16 g from 1.52 g), m.p. 242–243 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1651 (C=N), 2219 (CN), 3433 (NH$_2$) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 5.14 (s, 2 H, CH$_2$), 7.04 (d, *J* = 2.2 Hz, 1 H, ArH), 7.11 (d, *J* = 2.2 Hz, 1 H, ArH), 7.37–7.43 (m, 2 H, ArH), 7.56 (s, 1 H, =CH), 7.65 (s, 1 H, ArH), 7.98–8.02 (m, 2 H, ArH), 8.10 (s, 2 H, NH$_2$) ppm. ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ = 47.3, 106.8, 111.0, 114.2, 116.1, 116.8, 117.1, 124.8, 129.8, 129.9, 130.1, 147.4, 162.3, 162.4, 164.5, 165.7 ppm. MS (ES+): *m*/*z* = 310.1 [M + 1]$^+$. HRMS (EI): calcd. for $C_{16}H_{12}FN_5O$ 309.1026; found 309.1027.

2-[(2-Amino-1*H*-imidazol-1-yl)methyl]-3-[3-(4-methylphenyl)-isoxazol-5-yl]prop-2-enenitrile (3q): Ethyl acetate/methanol (18:1); white solid (1.20 g from 1.62 g), m.p. 215–217 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1664 (C=N), 2225 (CN), 3288 (NH$_2$) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 2.36 (s, 3 H, CH$_3$), 5.24 (s, 2 H, CH$_2$), 7.02 (s, 1 H, ArH), 7.11 (s, 1 H, ArH), 7.34 (d, *J* = 7.7 Hz, 2 H, ArH), 7.50 (s, 1 H, =CH), 7.74 (s, 1 H, ArH), 7.80 (d, *J* = 7.7 Hz, 2 H, ArH), 8.23 (s, 2 H, NH$_2$) ppm. ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ = 21.5, 47.1, 106.5, 110.7, 114.0, 116.0, 116.6, 125.2, 127.1, 130.1, 130.2, 141.0, 147.3, 162.9, 164.1 ppm. MS (ES+): *m*/*z* = 306.1 [M + 1]$^+$. HRMS (DART, as ES+): calcd. for $C_{17}H_{16}N_5O$ 306.13548; found 306.13556.

2-[(2-Amino-1*H*-imidazol-1-yl)methyl]-3-(5-methyl-3-phenyl-isoxazol-4-yl)prop-2-enenitrile (3u): Ethyl acetate/methanol (19:1); white solid (1.03 g from 1.59 g), m.p. 131–133 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1664 (C=N), 2217 (CN), 3367 (NH$_2$) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 1.91 (s, 3 H, CH$_3$), 4.84 (s, 2 H, CH$_2$), 5.60 (br. s, 2 H, NH$_2$), 6.49 (d, *J* = 1.4 Hz, 1 H, ArH), 6.70 (d, *J* = 1.4 Hz, 1 H, ArH), 7.02 (s, 1 H, =CH), 7.55 (d, *J* = 5.6 Hz, 3 H, ArH), 7.64–7.67 (m, 2 H, ArH) ppm. ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ = 13.7, 46.7, 110.3, 115.3, 115.7, 122.1, 128.8, 130.0, 131.2, 135.6, 149.8, 169.5 ppm. MS (ES+): *m*/*z* = 306.1 [M + 1]$^+$. HRMS (DART, as ES+): calcd. for $C_{17}H_{16}N_5O$ 306.13548; found 306.13489.

General Procedure for the One-Pot Synthesis of 6-(Hetarylmethyl)-imidazo[1,2-*a*]pyrimidin-7-ylamines 4n–t,v from 2n–t,v: A similar protocol to that described for the aforementioned synthesis of **3** was used, except the heating of the reaction mixture in the presence of HCl was extended to 30 min.

General Procedure for the Synthesis of 6-(Arylmethyl)imidazo[1,2-*a*]pyrimidin-7-ylamines 4a–m,u as Exemplified for 4a: Compound **3a** (0.50 g, 2.23 mmol) was added to a solution of NaOMe in methanol [prepared by dissolving Na (0.11 g, 4.5 mmol) in methanol (5 mL)], and the mixture was heated at reflux for 1 h. Upon completion, excess methanol was removed under vacuum, and water (50 mL) was added to the residue. This mixture was extracted with ethyl acetate (3 × 15 mL), the organic layers were combined, dried with Na_2SO_4 and concentrated to afford the crude product. Purification of the crude material by silica gel column chromatography employing ethyl acetate/methanol (19:1, v/v) as eluent furnished the desired product **4a** in 72% yield as a white solid (0.36 g).

6-Benzylimidazo[1,2-*a*]pyrimidin-7-ylamine (4a): M.p. 225–227 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1669 (C=N), 3427 (NH$_2$) cm^{-1}. ^{1}H NMR ([D$_6$]-DMSO, 300 MHz): δ = 3.79 (s, 2 H, CH$_2$), 6.37 (s, 2 H, NH$_2$), 7.11 (d, *J* = 1.4 Hz, 1 H, ArH), 7.17–7.30 (m, 6 H, ArH), 7.89 (s, 1 H, ArH) ppm. ^{13}C NMR (CDCl$_3$ + [D$_6$]DMSO, 75 MHz): δ = 32.5, 107.7, 110.0, 125.3, 127.3, 127.4, 129.5, 131.2, 135.9, 147.5, 155.9 ppm. MS (ES+): *m*/*z* = 225.3 [M + 1]$^+$. HRMS (EI): calcd. for $C_{13}H_{12}N_4$ 224.1062; found 224.1063.

6-(2-Chlorobenzyl)imidazo[1,2-*a*]pyrimidin-7-ylamine (4b): Ethyl acetate/methanol (19:1); white solid (0.53 g from 0.68 g), m.p. 188–191 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1663 (C=N), 3402 (NH$_2$) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 3.88 (s, 2 H, CH$_2$), 6.74 (br. s, 2 H, NH$_2$), 7.10 (d, *J* = 1.2 Hz, 1 H, ArH), 7.33–7.36 (m, 4 H, ArH), 7.50–7.53 (m, 1 H, ArH), 7.75 (s, 1 H, ArH) ppm. ^{13}C NMR ([D$_6$]-DMSO, 75 MHz): δ = 31.9, 109.9, 110.1, 128.1, 129.3, 130.1, 131.1, 131.7, 132.7, 134.0, 135.7, 149.0, 157.5 ppm. MS (ES+): *m*/*z* = 259.4 [M + 1]$^+$. HRMS (EI): calcd. for $C_{13}H_{11}ClN_4$ 258.0672; found 258.0674.

6-(2-Fluorobenzyl)imidazo[1,2-*a*]pyrimidin-7-ylamine (4c): Ethyl acetate/methanol (19:1); white solid (0.51 g from 0.73 g), m.p. 197–200 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1669 (C=N), 3422 (NH$_2$) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 3.84 (s, 2 H, CH$_2$), 6.73 (s, 2 H, NH$_2$), 7.11–7.36 (m, 6 H, ArH), 7.97 (s, 1 H, ArH) ppm. ^{13}C NMR ([D$_6$]-DMSO, 75 MHz): δ = 27.4, 110.0, 110.3, 115.9, 116.1, 125.2, 129.5, 131.2, 131.7, 133.1, 149.2, 157.6 ppm. MS (ES+): *m*/*z* = 243.4 [M + 1]$^+$. HRMS (EI): calcd. for $C_{13}H_{11}FN_4$ 242.0968; found 242.0967.

6-(4-Chlorobenzyl)imidazo[1,2-*a*]pyrimidin-7-ylamine (4e): Ethyl acetate/methanol (19:1); a white solid (0.38 g from 0.55 g), m.p. 172–173 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1667 (C=N), 3471 (NH$_2$) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 3.82 (s, 2 H, CH$_2$), 6.63 (s, 2 H, NH$_2$), 7.12 (s, 1 H, ArH), 7.31–7.36 (s, 5 H, ArH), 8.15 (s, 1 H, ArH) ppm. ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ = 32.8, 109.8, 111.4, 128.9, 131.2, 131.6, 133.4, 137.8, 149.1, 157.4 ppm. MS (ES+): *m*/*z* = 259.4 [M + 1]$^+$. HRMS (EI): calcd. for $C_{13}H_{11}ClN_4$ 258.0672; found 258.0669.

6-(4-Fluorobenzyl)imidazo[1,2-*a*]pyrimidin-7-ylamine (4f): Ethyl acetate/methanol (19:1); white solid (0.45 g from 0.59 g), m.p. 165–168 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1663 (C=N), 3452 (NH$_2$) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 3.80 (s, 2 H, CH$_2$), 6.66 (s, 2 H, NH$_2$), 7.12–7.17 (m, 3 H, ArH), 7.31–7.36 (m, 3 H, ArH), 8.13 (s, 1 H, ArH) ppm. ^{13}C NMR ([D$_6$]DMSO, 50 MHz): δ = 32.7, 109.8, 111.8, 115.6, 115.9, 131.1, 131.2, 133.3, 134.8, 149.1, 157.5, 159.9, 163.1 ppm. MS (ES+): *m*/*z* = 243.4 [M + 1]$^+$. HRMS (EI): calcd. for $C_{13}H_{11}FN_4$ 242.0968; found 242.0963.

6-(4-Methylbenzyl)imidazo[1,2-*a*]pyrimidin-7-ylamine (4g): Ethyl acetate/methanol (19:1); white solid (0.51 g from 0.61 g), m.p. 263–

265 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1676 (C=N), 3460 (NH_2) cm^{-1}. ^1H NMR ([D_6]DMSO, 300 MHz): δ = 2.25 (s, 3 H, CH_3), 3.74 (s, 2 H, CH_2), 6.60 (s, 2 H, NH_2), 7.09–7.18 (m, 5 H, ArH), 7.34 (s, 1 H, ArH), 8.05 (s, 1 H, ArH) ppm. ^{13}C NMR ([D_6]DMSO, 75 MHz): δ = 21.3, 109.9, 112.2, 129.4, 129.7, 131.1, 133.2, 135.6, 136.1, 149.2, 157.7 ppm. MS (ES+): *m*/*z* = 239.4. [M + 1]$^+$. HRMS (EI): calcd. for $C_{14}H_{14}N_4$ 238.1218; found 238.1211.

6-(4-Methoxybenzyl)imidazo[1,2-*a*]pyrimidin-7-ylamine (4h): Ethyl acetate/methanol (18:1); white solid (0.52 g from 0.71 g), m.p. 245–247 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1667 (C=N), 3427 (NH_2) cm^{-1}. ^1H NMR ([D_6]DMSO, 300 MHz): δ = 3.72 (s, 3 H, OCH_3), 3.91 (s, 2 H, CH_2), 6.87 (d, *J* = 8.4 Hz, 2 H, ArH), 7.12 (d, *J* = 8.3 Hz, 2 H, ArH), 7.57 (s, 1 H, ArH), 7.80 (s, 1 H, ArH), 8.62 (s, 1 H, ArH) ppm. ^{13}C NMR ([D_6]DMSO, 50 MHz): δ = 33.5, 55.5, 111.8, 114.5, 118.7, 130.3, 130.8, 134.4, 135.2, 147.0, 150.9, 158.4 ppm. MS (ES+): *m*/*z* = 255.2 [M + 1]$^+$. HRMS (EI): calcd. for $C_{14}H_{14}N_4O$ 254.1168; found 254.1169.

6-(2,4-Dichlorobenzyl)imidazo[1,2-*a*]pyrimidin-7-ylamine (4i): Ethyl acetate/methanol (20:1); white solid (0.45 g from 0.63 g), m.p. 214–219 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1667 (C=N), 3374 (NH_2) cm^{-1}. ^1H NMR ([D_6]DMSO, 300 MHz): δ = 3.85 (s, 2 H, CH_2), 6.75 (s, 2 H, NH_2), 7.09 (s, 1 H, ArH), 7.33–7.35 (m, 2 H, ArH), 7.43–7.45 (m, 1 H, ArH), 7.69 (s, 1 H, ArH), 7.79 (s, 1 H, ArH) ppm. ^{13}C NMR ([D_6]DMSO, 50 MHz): δ = 31.5, 109.8, 110.0, 128.3, 129.6, 131.1, 132.8, 132.9, 133.0, 134.9, 135.1, 149.1, 157.5 ppm. MS (ES+): *m*/*z* = 294.0 [M + 1]$^+$. HRMS (EI): calcd. for $C_{13}H_{10}Cl_2N_4$ 292.0283; found 292.0281.

6-(2,6-Dichlorobenzyl)imidazo[1,2-*a*]pyrimidin-7-ylamine (4j): Ethyl acetate/methanol (20:1); white solid (0.39 g from 0.53 g), m.p. 255–257 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1640 (C=N), 3424 (NH_2) cm^{-1}. ^1H NMR ([D_6]DMSO, 300 MHz): δ = 4.19 (s, 2 H, CH_2), 7.39–7.45 (m, 1 H, ArH), 7.55–7.58 (m, 3 H, ArH), 7.77 (s, 1 H, ArH), 8.06 (s, 1 H, ArH) ppm. ^{13}C NMR ([D_6]DMSO, 75 MHz): δ = 30.5, 112.1, 115.7, 129.4, 130.5, 133.0, 134.0, 135.9, 146.8, 150.9 ppm. MS (ES+): *m*/*z* = 293.4 [M + 1]$^+$. HRMS (EI): calcd. for $C_{13}H_{10}Cl_2N_4$ 292.0283; found 292.0277.

6-(3,4-Dimethoxybenzyl)imidazo[1,2-*a*]pyrimidin-7-ylamine (4k): Ethyl acetate/methanol (17:1); white solid (0.44 g from 0.65 g), m.p. 225–227 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1665 (C=N), 3448 (NH_2) cm^{-1}. ^1H NMR ([D_6]DMSO, 300 MHz): δ = 3.72 (s, 6 H, 2 × OCH_3), 3.90 (s, 2 H, CH_2), 6.72 (s, 1 H, ArH), 6.83–6.89 (m, 2 H, ArH), 7.58 (s, 1 H, ArH), 7.81 (s, 1 H, ArH), 8.59 (s, 1 H, ArH) ppm. ^{13}C NMR ([D_6]DMSO, 50 MHz): δ = 34.4, 56.3, 112.2, 112.8, 113.6, 119.1, 121.7, 131.6, 134.8, 135.6, 147.4, 148.3, 149.6, 151.3 ppm. MS (ES+): *m*/*z* = 285.6 [M + 1]$^+$. HRMS (EI): calcd. for $C_{15}H_{16}N_4O_2$ 284.1273; found 284.1274.

6-(2-Thienylmethyl)imidazo[1,2-*a*]pyrimidin-7-ylamine (4l): Ethyl acetate/methanol (19:1); white solid (0.47 g from 0.66 g), m.p. 237–240 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1655 (C=N), 3431 (NH_2) cm^{-1}. ^1H NMR ([D_6]DMSO, 300 MHz): δ = 4.21 (s, 2 H, CH_2), 6.90–6.91 (d, *J* = 2.5 Hz, 1 H, ArH), 6.95–6.98 (m, 1 H, ArH), 7.35–7.37 (m, 1 H, ArH), 7.60 (d, *J* = 1.3 Hz, 1 H, ArH), 7.84 (d, *J* = 1.3 Hz, 1 H, ArH), 8.79 (s, 1 H, ArH) ppm. ^{13}C NMR ([D_6]DMSO, 75 MHz): δ = 29.0, 112.0, 118.0, 125.4, 126.6, 127.7, 134.7, 135.4, 141.8, 147.0, 150.7 ppm. MS (ES+): *m*/*z* = 231.3 [M + 1]$^+$. HRMS (EI): calcd. for $C_{11}H_{10}N_4S$ 230.0626; found 230.0629.

6-(2-Furylmethyl)imidazo[1,2-*a*]pyrimidin-7-ylamine (4m): Ethyl acetate/methanol (19:1); white solid (0.39 g from 0.58 g), m.p. 234–236 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1656 (C=N), 3431 (NH_2) cm^{-1}. ^1H NMR ([D_6]DMSO, 300 MHz): δ = 4.03 (s, 2 H, CH_2), 6.18 (d, *J* = 2.7 Hz, 1 H, ArH), 6.38–6.40 (m, 1 H, ArH), 7.54 (s, 1 H, ArH), 7.60 (d, *J* = 1.1 Hz, 1 H, ArH), 7.84 (d, *J* = 1.1 Hz, 1 H, ArH), 8.71 (s, 1 H, ArH) ppm. ^{13}C NMR ([D_6]DMSO, 75 MHz): δ = 27.8, 107.7, 111.3, 112.0, 115.7, 134.7, 135.6, 142.9, 147.1, 150.8, 152.3 ppm. MS (ES+): *m*/*z* = 215.4 [M + 1]$^+$. HRMS (EI): calcd. for $C_{11}H_{10}N_4S$ 214.0855; found 214.0863.

6-[(3-Phenylisoxazol-5-yl)methyl]imidazo[1,2-*a*]pyrimidin-7-ylamine (4n): Ethyl acetate/methanol (15:1); white solid (1.12 g from 1.52 g), m.p. 250–253 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1671 (C=N), 3432 (NH_2) cm^{-1}. ^1H NMR ([D_6]DMSO, 200 MHz): δ = 4.11 (s, 2 H, CH_2), 6.80 (s, 3 H, ArH and NH_2), 7.15 (s, 1 H, ArH), 7.41 (s, 1 H, ArH), 7.44–7.47 (m, 3 H, ArH), 7.82–7.85 (m, 2 H, ArH), 8.42 (s, 1 H, ArH) ppm. ^{13}C NMR ([D_6]DMSO, 50 MHz): δ = 26.2, 101.5, 107.5, 110.3, 127.4, 129.5, 130.0, 131.0, 131.8, 134.8, 149.6, 157.6, 162.8, 171.7 ppm. MS (ES+): *m*/*z* = 292.6 [M + 1]$^+$. HRMS (EI): calcd. for $C_{16}H_{13}N_5O$ 291.1120; found 291.1116.

6-{[3-(2-Chlorophenyl)isoxazol-5-yl]methyl}imidazo[1,2-*a*]pyrimidin-7-ylamine (4o): Ethyl acetate/methanol (15:1); white solid (1.14 g from 1.60 g), 160 °C (decomp.). IR (KBr): $\tilde{\nu}_{max}$ = 1673 (C=N), 3434 (NH_2) cm^{-1}. ^1H NMR ([D_6]DMSO, 300 MHz): δ = 4.20 (s, 2 H, CH_2), 6.78 (s, 1 H, ArH), 6.87 (s, 2 H, NH_2), 7.15 (s, 1 H, ArH), 7.43–7.55 (m, 3 H, ArH), 7.60–7.68 (m, 2 H, ArH), 8.50 (s, 1 H, ArH) ppm. ^{13}C NMR ([D_6]DMSO, 75 MHz): δ = 25.9, 104.3, 107.3, 110.1, 128.4, 128.5, 131.1, 131.5, 131.7, 132.2, 132.4, 134.7, 157.4, 161.2, 170.8 ppm. MS (ES+): *m*/*z* = 326.1 [M + 1]$^+$. HRMS (EI): calcd. for $C_{16}H_{12}ClN_5O$ 325.0730; found 325.0737.

6-{[3-(4-Fluorophenyl)isoxazol-5-yl]methyl}imidazo[1,2-*a*]pyrimidin-7-ylamine (4p): Ethyl acetate/methanol (15:1); white solid (0.84 g from 1.13 g), 200 °C (decomp.). IR (KBr): $\tilde{\nu}_{max}$ = 1662 (C=N), 3413 (NH_2) cm^{-1}. ^1H NMR ([D_6]DMSO, 300 MHz): δ = 4.15 (s, 2 H, CH_2), 6.81 (s, 2 H, NH_2), 6.84 (s, 1 H, ArH), 7.29–7.35 (m, 3 H, ArH), 7.87–7.92 (m, 3 H, ArH), 8.46 (s, 1 H, ArH) ppm. ^{13}C NMR ([D_6]DMSO, 75 MHz): δ = 25.8, 101.1, 107.2, 116.4, 116.7, 129.3, 129.4, 131.2, 134.4, 157.2, 161.5, 165.2, 171.5 ppm. MS (ES+): *m*/*z* = 310.1 [M + 1]$^+$. $C_{16}H_{12}FN_5O$ (309.1026): C 62.13, H 3.91, N 22.64; found C 62.33, H 4.12, N 22.53.

6-{[3-(4-Methylphenyl)isoxazol-5-yl]methyl}imidazo[1,2-*a*]-pyrimidin-7-ylamine (4q): Ethyl acetate/methanol (15:1); white solid (0.83 g from 1.21 g), m.p. 220–222 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1668 (C=N), 3426 (NH_2) cm^{-1}. ^1H NMR ([D_6]DMSO, 300 MHz): δ = 2.33 (s, 3 H, CH_3), 4.11 (s, 2 H, CH_2), 6.77 (s, 1 H, ArH), 6.82 (s, 2 H, NH_2), 7.17 (s, 1 H, ArH), 7.28 (d, *J* = 6.9 Hz, 2 H, ArH), 7.42 (s, 1 H, ArH), 7.73 (d, *J* = 7.1 Hz, 2 H, ArH), 8.44 (s, 1 H, ArH) ppm. ^{13}C NMR ([D_6]DMSO, 75 MHz): δ = 21.4, 25.8, 101.0, 107.1, 109.9, 126.3, 126.9, 130.1, 134.4, 140.3, 149.1, 157.2, 162.3, 171.1 ppm. MS (ES+): *m*/*z* = 306.1 [M + 1]$^+$. HRMS (DART, as ES+): calcd. for $C_{17}H_{16}N_5O$ 306.1355; found 306.1339.

4-{5-[(7-Aminoimidazo[1,2-*a*]pyrimidin-6-yl)methyl]isoxazol-3-yl}phenol (4r): Ethyl acetate/methanol (15:1); white solid (0.50 g from 1.10 g), 225 °C (decomp.). IR (KBr): $\tilde{\nu}_{max}$ = 1672 (C=N), 3431 (NH_2) cm^{-1}. ^1H NMR ([D_6]DMSO, 300 MHz): δ = 4.09 (s, 2 H, CH_2), 6.70 (s, 1 H, ArH), 6.80 (s, 2 H, NH_2), 6.87 (d, *J* = 7.8 Hz, 2 H, ArH), 7.16 (s, 1 H, ArH), 7.42 (s, 1 H, ArH), 7.64 (d, *J* = 6.9 Hz, 2 H, ArH), 8.42 (s, 1 H, ArH) ppm. ^{13}C NMR ([D_6]DMSO, 75 MHz): δ = 25.9, 101.0, 107.6, 110.1, 116.5, 119.9, 128.7, 131.1, 134.5, 149.2, 157.5, 160.0, 162.4, 170.7 ppm. MS (ES+): *m*/*z* = 308.5 [M + 1]$^+$. $C_{16}H_{13}N_5O_2$ (307.1069): calcd. C 62.53, H 4.26, N 22.79; found C 62.72, H 4.49, N 22.81.

6-{[3-(2,4-Dichlorophenyl)isoxazol-5-yl]methyl}imidazo[1,2-*a*]-pyrimidin-7-ylamine (4s): Ethyl acetate/methanol (15:1); white solid (0.81 g from 1.20 g), m.p. 135–138 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1651

(C=N), 3424 (NH_2) cm^{-1}. ^1H NMR ([D_6]DMSO, 300 MHz): δ = 4.29 (s, 2 H, CH_2), 6.89 (s, 2 H, NH_2), 7.59–7.85 (m, 6 H, ArH), 8.67 (s, 1 H, ArH) ppm. ^{13}C NMR ([D_6]DMSO, 75 MHz): δ = 25.9, 104.9, 111.4, 112.8, 119.2, 127.6, 128.9, 130.8, 133.1, 133.6, 136.1, 136.3, 145.5, 160.7, 161.2, 170.1 ppm. MS (ES+): *m*/*z* = 360.1 $[M + 1]^+$. HRMS (EI): calcd. for $C_{16}H_{11}Cl_2N_5O$ 359.0341; found 359.0344.

6-[(5-Phenylisoxazol-3-yl)methyl]imidazo[1,2-*a*]pyrimidin-7-ylamine (4t): Ethyl acetate/methanol (15:1); white solid (0.63 g from 1.00 g), m.p. 122–125 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1649 (C=N), 3411 (NH_2) cm^{-1}. ^1H NMR ([D_6]DMSO, 300 MHz): δ = 4.08 (s, 2 H, CH_2), 7.02 (s, 1 H, ArH), 7.38–7.52 (m, 3 H, ArH), 7.63 (s, 1 H, ArH), 7.73 (s, 1 H, ArH), 7.83 (br. s, 2 H, ArH), 8.56 (s, 1 H, ArH) ppm. MS (ES+): *m*/*z* = 292.2 $[M + 1]^+$. HRMS (EI): calcd. for $C_{16}H_{13}N_5O$ 291.1120; found 291.1119.

6-[(5-Methyl-3-phenylisoxazol-4-yl)methyl]imidazo[1,2-*a*]pyrimidin-7-ylamine (4u): Ethyl acetate/methanol (15:1); white solid (0.59 g from 0.81 g), m.p. 136–138 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1666 (C=N), 3413 (NH_2) cm^{-1}. ^1H NMR ([D_6]DMSO, 300 MHz): δ = 2.40 (s, 3 H, CH_3), 3.62 (s, 2 H, CH_2), 6.87 (s, 2 H, NH_2), 7.10 (s, 1 H, ArH), 7.33 (s, 1 H, ArH), 7.47 (s, 5 H, ArH), 7.89 (s, 1 H, ArH) ppm. ^{13}C NMR ([D_6]DMSO, 75 MHz): δ = 11.3, 21.7, 108.2, 110.0, 110.1, 127.9, 129.5, 130.2, 132.1, 148.7, 157.5, 162.4, 169.0 ppm. MS (ES+): *m*/*z* = 306.2 $[M + 1]^+$. HRMS (EI): calcd. for $C_{17}H_{15}N_5O$ 305.1277; found 305.1281.

6-[(1,5-Diphenyl-1*H*-pyrazol-3-yl)methyl]imidazo[1,2-*a*]pyrimidin-7-ylamine (4v): Ethyl acetate/methanol (17:1); white solid (0.67 g from 1.48 g), m.p. 191–193 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1664 (C=N), 3351 (NH_2) cm^{-1}. ^1H NMR ([D_6]DMSO, 300 MHz): δ = 3.90 (s, 2 H, CH_2), 6.58 (s, 1 H, ArH), 6.86 (s, 2 H, NH_2), 7.22–7.44 (m, 12 H, ArH), 8.38 (s, 1 H, ArH) ppm. ^{13}C NMR ([D_6]DMSO, 75 MHz): δ = 27.2, 108.2, 110.7, 111.7, 116.2, 125.7, 128.2, 128.9, 129.2, 129.6, 130.5, 133.7, 140.2, 144.1, 150.0, 158.8 ppm. MS (ES+): *m*/*z* = 367.3 $[M + 1]^+$. HRMS (EI): calcd. for $C_{22}H_{18}N_6$ 366.1593; found 366.1601.

Typical Procedure for Acetylation of 4b: Ac_2O (0.18 mL, 1.93 mmol) was added dropwise to a mixture of compound **4b** (0.25 g, 0.97 mmol) and pyridine (0.50 mL) at 0 °C, and the reaction mixture was stirred at room temperature for 3 h. On completion (as monitored by TLC, ca. 3 h), the reaction mixture was diluted with ethyl acetate (15 mL) and washed with water (20 mL). The organic layer was separated, whereas the aqueous layer was extracted with ethyl acetate (2 × 15 mL). The organic layers were combined, dried with Na_2SO_4, concentrated and purified by column chromatography on silica gel using ethyl acetate/methanol (40:1, v/v) as eluent to yield the pure product **5b** (0.29 g, 81%) as a white solid.

***N*-[6-(2-Chlorobenzyl)imidazo[1,2-*a*]pyrimidin-7-yl]acetamide (5b):** M.p. 212–214 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1665 (C=N and NHCO), 3451 (NH) cm^{-1}. ^1H NMR ([D_6]DMSO, 300 MHz): δ = 2.10 (s, 3 H, CH_3), 4.07 (s, 2 H, CH_2), 7.31–7.58 (m, 4 H, ArH), 7.82 (s, 1 H, ArH), 8.33 (s, 1 H, ArH), 8.46 (s, 1 H, ArH) ppm. MS (ES+): *m*/*z* = 301.2 $[M + 1]^+$. $C_{15}H_{13}ClN_4O$ (300.0778): calcd. C 59.91, H 4.36, N 18.63; found C 60.12, H 4.48, N 18.56.

Supporting Information (see footnote on the first page of this article): Copies of the ^1H and ^{13}C NMR spectra of all new compounds.

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