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A simple, economical, and environmentally benign protocol for the synthesis of 2-amino-3,5-dicarbonitrile-6-sulfanylpyridines at ambient temperature

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A simple, economical, and environmentally benign protocol has been described for one-pot synthesis of medicinally privileged 2-amino-3,5-dicarbonitrile-6-sulfanylpyridines by three-component condensation between aldehyde, malononitrile, and thiol using diethylamine as a catalyst. Ambient temperature and avoidance of conventional work-up as well as purification procedure qualify this cost-effective protocol for “green synthesis.”

Keywords: multicomponent reactions; diethylamine; pyridine-3,5-dicarbonitriles; organocatalyst; green chemistry

1. Introduction

The main issue in modern organic chemistry which deals with the synthesis of organic compounds having diverse applications is mainly aimed at improvement in atom as well as cost efficiency, avoidance of toxic reagents, and reduction in waste with responsible utilization of natural resources. In this context, possibility of performing multicomponent reactions is of relevance both from economical as well as from ecological point of view (1–4). The importance of multicomponent reactions increases many fold when they provide an easy access to “privileged medicinal scaffolds” obeying the demands of “green chemistry” or of an “ideal synthesis” (5). Pyridine-3,5-dicarbonitrile constitutes one such medicinally privileged scaffold (Figure 1A), and diversification at positions C2, C4, and C6 of the pyridine core results in a great number of compounds with useful biological activities. For instance, pyridine-3,5-dicarbonitriles with amino and sulfanyl moieties at positions C2 and C6, respectively and with aryl or hetero-aryl substitution at C4 have been found to be a highly useful pattern. The literature survey revealed that such penta-substituted pyridines (Figure 1) exhibit diverse medicinal properties such as antibacterial (6), anticancer (7), potassium channel opener for treatment of urinary incontinence (8), anti-hepatitis B virus infection (9). Parkinson’s disease, hypoxia, asthma, cancer, kidney diseases, etc. (10–12). A few other compounds of this class are used in the treatment of Creutzfeldt disease in humans and bovine spongiform encephalopathy as well as scrapie in sheep (13–15). Such a wide range of applications of pyridine-3,5-dicarbonitriles have inspired many researchers to develop efficient methods for their synthesis.

As regards the synthesis of pyridine-3,5-dicarbonitriles is concerned, a few multistep protocols have been reported earlier (16–18). However, one-pot, three-component condensation between aldehyde, malononitrile, and thiol has been the most exploited pathway. This multicomponent condensation has been delineated to proceed via Knoevenagel-thia-Michael cascade pathway (Scheme 1b; 19, 20). As Knoevenagel as well as Michael addition reactions are usually catalyzed by bases, a range of bases such as Et3N, DABCO (20, 21), piperidine, TBAH (22), DBU (23), {[bmim] OH} (24), KF-Al2O3 (25), nanocrystalline-MgO (26), ethanolic KOH (27), K2CO3–K2MnO4 (28), etc. have been reported for their synthesis. As opposed to the usual base catalysis, their synthesis has also been reported using Lewis as well as Bronsted acid catalysts (29–32) or by using CuI, silica-nano particles (33, 34), molecular sieves (35), IBX (36), etc. as catalysts. Each of these methods has its own merits. However, a few of these protocols require expensive catalyst or long reaction times. On the other hand, a few other protocols are associated with the drawback as regards the formation of corresponding dihydropyridine, 6, as an
undesired product \((21, 28)\). Interestingly, most of the reported protocols with variation in the catalyst used require elevated temperature and to the best of our knowledge, there are only three protocols that are operable at ambient temperature \((24, 31, 37)\). Keeping in view the growing medicinal importance of pyridine-3,5-dicarbonitriles and our continued interest in the development of eco-benign synthetic methodologies \((38–44)\), we surmised that introduction of an energy-efficient, eco-safe, and easily adaptable protocol for their synthesis at ambient temperature is highly desirable (Scheme 1a).

2. Results and discussion

For the preliminary studies, 2-amino-3,5-dicarbonitrile-4-phenyl-6-sulfanyl-pyridine, \(7a\), was chosen as a model compound. Accordingly, benzaldehyde, malononitrile, and thiophenol were chosen as substrates (1:2:1 equiv.) and a few model reactions were performed employing potassium phosphate, borax, polyvinyl pyridine (PVP) as well as Amberlite IRA-400 (OH\(^-\) form) as catalysts. The choice of potassium phosphate as well as borax was based on the mechanism of the reaction as well as on the early reports in using these catalysts in Knoevenagel as well as in thia-Michael addition reactions \((38, 39, 45)\). On the other hand, the choice of PVP as well as Amberlite IRA-400 (OH\(^-\) form) was concerned with the possibility of their reuse. The results of the model reactions are summarized in Table 1. It was observed that, with the choice of PVP as well as IRA-400 (OH\(^-\) form) was concerned with the possibility of their reuse. The results of the model reactions are summarized in Table 1. It was observed that, with the choice of PVP as well as IRA-400 (OH\(^-\) form), the reaction remained arrested at Knoevenagel condensation stage to furnish benzylidene malononitrile, \(4a\), as the major product. On the other hand, with the choice of potassium phosphate as well as borax as catalysts, resultant product was identified to be a mixture of dihydropyridine, \(6a\), and its oxidation product, namely pyridine-3,5-dicarbonitrile, \(7a\), in nearly 2:1 proportion (\(^1\)H NMR). It is noteworthy that, in situ
oxidation of dihydropyridine, 6a, to pyridine-3,5-dicarbonitrile, 7a, has been proposed earlier to proceed by two different pathways, namely aerobic oxidation or by oxidation with the initially formed Knoevenagel condensation product, 4a (Scheme 1b). Furthermore, for the reaction to follow the second path of oxidation, the presence of an extra equivalent of Knoevenagel condensation product was recommended as essential (21, 22). Hence, the aforementioned model reactions were then repeated using aldehyde, malononitrile, and thiophenol in 2:3:1 proportion using potassium phosphate as well as borax as catalysts. However, we did not observe any significant change in the proportion of 6a:7a, in the isolated product. So also, stirring the reaction mixture in open air for longer time at room temperature as well as at reflux temperature was not found to be useful in obtaining 7a, exclusively (entries 4 and 5; Table 1). This initial failure prompted us to screen another catalyst for the exclusive synthesis of 7a, at ambient temperature.

Diethylamine is an inexpensive, nontoxic, and easy to handle organic base available commercially. The first report on the use of diethylamine in promoting Knoevenagel condensation appeared in 1940s (46). However, to the best of our knowledge, its use as a catalyst in multicomponent reactions remained ignored. In fact, we have recently demonstrated the use of diethylamine in multicomponent synthesis of 2-amino-3-cyano-4H-chromenes employing Knoevenagel-phospha-Michael as well as Knoevenagel-carba-Michael cascade pathway (42, 43). Since the synthesis of pyridine-3,5-dicarbonitriles, 7a, involves Knoevenagel-carba as well as thia-Michael cascade pathway, it was quite logical for us to examine the use of diethylamine in this multicomponent reaction. To begin with, a model reaction was carried out using the same substrate combination (2:3:1 equiv.), diethylamine (20 mol%) as the catalyst and ethanol (1 mL) as a solvent. Upon addition of the catalyst, slightly exothermic reaction took place and upon completion of the reaction, thin layer chromatography (TLC) examination showed the formation of two main products, 6a and 7a. Stirring was continued in open air and it was noticed that oxidation of 6a to 7a proceeds slowly (TLC). After four hours, more ethanol was added to the reaction mixture and the resultant solid was filtered, dried, and washed using hexane-chloroform mixture (8:2, v/v, 20 mL). The resultant product was identified to be pyridine-3,5-dicarbonitrile, 7a, (1H NMR) in acceptable yield. Following this initial success, from economical as well as atom-economical point of view, the reaction was repeated using the same reactants in 1:2:1 proportion. The reaction proceeded smoothly and upon completion of the reaction followed by workup, we were truly gratified to notice the formation of desired pyridine-3,5-dicarbonitrile, 7a, in nearly the same yield (80%). On the other hand, when the reaction was repeated using 10 mol% of diethylamine as the catalyst-desired product, 7a was obtained in lower yield (Table 1, entry 12).

Encouraged by this initial success, we next planned to explore the scope as well as the generality of the reaction conditions in the synthesis of various pyridine-3,5-dicarbonitriles. Accordingly, a series of substituted aromatic aldehydes and thiols were screened. Results summarized in Table 2 reveal that the protocol developed is compatible with the aromatic aldehydes containing electron-withdrawing as

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**Table 1. Optimization of reaction conditions for the synthesis of 7a.**

| Entry | Catalyst (mol%/g) | Time (h) | 5a (%) | 6a (%) |
|-------|------------------|----------|--------|--------|
| 1     | K₃PO₄ (10)       | 3⁴       | 60⁴    | 40⁴    |
| 2     | K₃PO₄ (20)       | 6⁴       | 60     | 40     |
| 3     | K₃PO₄ (20)       | 3⁴, 5    | 70     | 30     |
| 4     | K₃PO₄ (20)       | 6       | 65     | 35     |
| 5     | K₃PO₄ (20)       | 3⁴, 5    | 70     | 30     |
| 6     | Borax (10)       | 8¹       | 55     | 45     |
| 7     | PVP (1 g)        | 8¹       | –      | –¹     |
| 8     | Amberlite IRA-400 (OH⁻) | 8¹     | –      | –¹     |
| 9     | Diethylamine (20) | 4.5¹     | –      | 82     |
| 10    | Diethylamine (20) | 4.5¹     | –      | 80     |
| 11    | Diethylamine (10) | 4.5¹     | –      | 65     |

¹Benzaldehyde, malononitrile, and thiophenol (1:2:1 equiv.), ethanol (1 mL), RT.
²Yield based on 1H NMR.
³Under reflux condition.
⁴Benzaldehyde, malononitrile, and thiophenol (2:3:1 equiv.), ethanol (1 mL).
⁵Product resulted was benzylidene malononitrile.
well as electron-donating groups and is also suitable for heteroaromatic aldehydes (Table 2, entries i, q, and u). To our delight, it also worked well with a wide variety of thiols such as 2-mercaptoethanol, benzylthiol, 4-methoxybenzyl thiol, 4-chloro thiophenol as well as 2-amino thiophenol (Table 2, entries r, q, l, o, and k). However, under the established reaction conditions, sterically hindered aldehydes like 2,6-dichloro as well as 2,6-dimethyl benzaldehyde furnished a mixture of corresponding dihydropyridine, 6, as well as pyridine, 7, while aliphatic aldehydes as well as thiols, except 2-mercaptoethanol, failed to furnish the corresponding pyridine-3,5-dicarbonitrile.

At this juncture two important observations are noteworthy.

(1) The basicity values of diethylamine, triethylamine, and piperidine are although very close, with the choice of triethylamine or piperidine as the catalyst, synthesis of pyridine-3,5-dicarbonitrile requires elevated temperature (21, 22). However, with the choice of diethylamine as the catalyst, we obtained the desired pyridine derivative at room temperature. In this context, based on our earlier experiences on aza, phospha as well as carba-Michael addition reaction studies (41–43), we propose that the initial exothermy that results upon addition of the catalyst to the reaction mixture might be one of the driving forces of the reaction. To give credence to this philosophy, three model reactions were performed using anisaldehyde, malononitrile, and thiophenol (1:2:1 equiv.) as substrates, diethylamine as the catalyst (20 mol%), and different amounts of ethanol as the solvent (1, 3, and 7 mL) when desired pyridine-3,5-dicarbonitrile, 7e, was obtained in 80%, 52%, and 40% yield, respectively. This reveals that with the increase in the amount of ethanol, possibly due to dissipation of

![Chemical structure](image-url)

**Table 2. Diethylamine catalyzed one-pot synthesis of pyridine-3,5-dicarbonitriles, 7a.**

| Product (7) | Aldehyde (1) R = | Thiol (3) R¹ = | Time (h) | Yield¹ (%) | Melting point (°C)B |
|------------|-----------------|----------------|----------|------------|---------------------|
| a          | Ph              | Ph             | 4.5      | 80         | 218–220 220–221²³  |
| b          | 4-Cl-Ph         | Ph             | 4.5      | 80         | 222–224 220–222²⁵  |
| c          | 4-Br-Ph         | Ph             | 4.5      | 82         | 256–258 256–258²³  |
| d          | 3-NO₂-Ph        | Ph             | 4        | 76         | 216–218 210–221²³  |
| e          | 4-OMe-Ph        | Ph             | 4        | 82         | 242–244 241–244²⁶  |
| f          | 4-Me-Ph         | Ph             | 4.5      | 80         | 208–210 208–210²³  |
| g          | 3,4-(MeO)₂-Ph   | Ph             | 4.5      | 78         | 230–232 228–230²⁰  |
| h          | 4-OH-Ph         | Ph             | 6        | 72         | 318–320 315–317²⁵  |
| i          | 2-Thiophenyl    | Ph             | 5        | 76         | 208–210 208–210²⁵  |
| j          | 4-CN-Ph         | 4-Me-Ph        | 4        | 80         | 215–218  –       |
| k          | 4-(CH₃)₂CH-Ph   | 2-NH₂-Ph       | 5        | 78         | 200–202  –       |
| l          | 4-(CH₃)₂CH-Ph   | 4-OMe-CH₂Ph    | 4.5      | 80         | 220–222  –       |
| m          | 4-(CH₃)₂CH-Ph   | 4-Me-Ph        | 5        | 78         | 226–228  –       |
| n          | 4-OMe-Ph        | 4-OMe-Ph       | 5        | 76         | 224–226  –       |
| o          | 4-(CH₃)₂CH-Ph   | 4-Cl-Ph        | 4        | 81         | 224–226  –       |
| p          | 4-(CH₃)₂CH-Ph   | 4-OMe-Ph       | 5        | 82         | 220–222  –       |
| q          | 2-Thiophenyl    | –CH₂-Ph        | 4.5      | 77         | 224–226  –       |
| r          | 3,4(OCH₂O)Ph    | –CH₂–CH₂–OH    | 4        | 78         | 248–250  –       |
| s          | 3,4(OCH₂O)Ph    | –CH₂-Ph        | 5        | 81         | 226–228  –       |
| t          | 3,4(OCH₂O)Ph    | 4-Me-Ph        | 4        | 78         | 256–258  –       |
| u          | Furfural        | 2-NH₂-Ph       | 5        | 67         | 226–228  –       |
| v          | 2,6-(CH₃)₂Ph   | 4-Cl-Ph        | 4        | 80²⁴       | 319–321 318–320²⁴ |
| w          | 2,6-(Cl)₂Ph    | 4-Me-Ph        | 4        | 78²⁵       | 214–215 216–218²¹ |

¹Reaction conditions: aldehyde, malononitrile, and thiol (1:2:1 equiv.), diethylamine (20 mol%), ethanol (1 mL), RT.
²All known products gave satisfactory spectral data (IR and ¹H NMR).
³Yields refer to corresponding dihydropyridine derivative.

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initially generated heat, percentage yield of 7e decreases.

(2) Oxidation of dihydropyridines, 6 to pyridines 7, has been proposed to proceed by either air oxidation pathway or by oxidation with arylidinemononitrile, 4 (21, 22). Based on our success in the synthesis of 7 in the absence of an extra equivalent of arylidinemononitrile, 4, we propose that oxidation of dihydropyridines, 6, to pyridines, 7, is a base-dependent reaction and with the choice of diethylamine as the catalyst, it proceeds by air oxidation pathway alone. In support of the same, finally we carried out a model reaction employing anisaldehyde, malononitrile, phenylsulfonyl acetonitrile, and thiophenol as substrates (1 equiv. each) and diethylamine (20 mol%) as catalyst. Upon completion of the reaction, instead of dihydropyridine, 6 or pyridine derivative, 8, the resultant product was identified to be 7e in very low yield (∼35 %, TLC; Scheme 2).

On the basis of these results, we inferred that (1) with the choice of diethylamine as a catalyst, oxidation of dihydropyridines, 6, to pyridines, 7, proceeds by air oxidation pathway alone and (2) the initial exothermy generated upon addition of diethylamine to the mixture of reactants plays an important role in the synthesis of pyridine-3,5-dicarbonitriles. In short, pKa values of diethylamine, triethylamine, and piperidine are although very close, their potential as catalysts is different. At this stage of work, we do not have any logical answer to explain this anomaly. In support of these claims, further studies are currently on in our laboratory.

3. Conclusion

In summary, we have developed an efficient protocol for multicomponent synthesis of medicinally privileged pyridine-3,5-dicarbonitriles using diethylamine as a catalyst. Easy commercial availability of the catalyst at extremely low cost, operational simplicity at ambient temperature, and avoidance of conventional work-up as well as purification procedure offer additional advantages to this energy-efficient protocol. To the best of our knowledge, literature to date contains no precedent for such a simple, economical, and environmentally conscious protocol for the synthesis of a wide range of pyridine-3,5-dicarbonitriles at ambient temperature.

4. Experimental

Typical procedure for the synthesis of 2-amino-4-aryl (or heteroaryl)-3,5-dicarbonitrile-6-sulfanylpyridines, 7:

To a well-stirred solution of an aromatic aldehyde (2 mmol), malononitrile (4 mmol) and thiophenol (2 mmol) in ethanol (1 mL) was added diethylamine (20 mol%) and stirring was continued. Upon completion of the reaction (TLC), ethanol (5 mL) was added and stirring was continued in open air till completion of oxidation. The resultant solid was filtered and washed successively using a mixture of cyclohexane:chloroform (80:20, v/v) and dried. It was found to be pure (TLC, NMR).

The spectral data of the new compounds are summarized below.

2-Amino-6-[(2-aminophenyl)sulfanyl]-4-[4-(propan-2-yl)phenyl]pyridine-3,5-dicarbonitrile, (7k): Solid; M.P. 215–218°C; IR (KBr): 3458, 3314, 2210, 1620, 1549, 1508, 1462, 1261, 1078, 1011 cm⁻¹; ¹H NMR (300 MHz, DMSO d₆): δ 1.27 (d, 6H, J = 6.9 Hz), 2.96 (m, 1H), 6.65 (t, 1H, J = 7.6 Hz), 6.82 (d, 1H, J = 8.06 Hz), 6.91 (brs, 2H, NH₂), 7.17 (t, 1H, J = 7.9 Hz), 7.20 (brs, 2H) 7.27 (d, 1H, J = 7.9 Hz), 7.38 (m, 4H, ArH) ppm; ¹³C NMR (75.4 MHz, DMSO d₆): δ 23.83 (CH₃ X 2), 33.99 (CH), 86.99 (ArC), 92.65 (ArC), 109.69, 115.30 (CN), 115.84 (ArCH), 126.85 (ArCH), 128.63 (ArCH), 129.30 (ArC), 131.12 (ArC), 131.78 (ArC), 137.51 (ArCH), 150.46 (ArC), 151.37 (ArC), 158.18 (ArC), 160.08 (ArC), 167.56 (ArC) ppm; high-resolution mass spectrum (HRMS): mass calculated for C₂₂H₁₉N₅S: 386.1441 (M + H) and 408.1258 (M + Na); Obs. mass: 386.1434 (M + H) and 408.1247 (M + Na).

2-Amino-6-[(4-methoxybenzyl)sulfanyl]-4-[4-(propan-2-yl)phenyl]pyridine-3,5-dicarbonitrile (7l): Solid; M.P. 200–202°C; IR (KBr): 3390, 3227, 3223, 2215, 1649, 1544, 1142, 1263, 1022 cm⁻¹; ¹H NMR (300 MHz,
DMSO $d_6$): $\delta$ 1.26 (d, 6H, $J = 7.3$ Hz), 2.95 (m, 1H), 3.73 (s, 3H), 4.37 (s, 2H), 6.76 (d, 2H, $J = 8.1$ Hz), 7.29–7.39 (m, 8H, ArCH + NH$_2$) ppm; $^{13}$C NMR (75.4 MHz, DMSO $d_6$): $\delta$ 32.38 (CH$_3$ X 2), 33.98 (CH), 34.09 (CH$_2$), 55.08 (OCH$_3$), 86.22 (ArC), 95.05 (ArC), 113.99 (ArCH), 115.05 (CN), 115.60 (CN), 126.81 (ArCH), 128.48 (ArCH), 128.59 (ArCH), 130.38 (ArCH), 131.08 (ArC), 157.91 (ArC), 158.99 (ArC), 167.94 (ArCH) ppm; HRMS: mass calculated for C$_{22}$H$_{19}$N$_4$OS: 407.1304 (M + H) and 409.1311 (M + Na); Obs. mass: 407.1300 (M + H) and 429.1210 (M + Na).

2-Amino-6-(2-hydroxyethyl)phenyl-3,5-dicarbonitrile (7s): Solid; M.P. 226$^\circ$C; IR (KBr): 3348, 3235, 2211, 1639, 1543, 1507, 1259, 1010 cm$^{-1}$; $^1$H NMR (300 MHz, DMSO $d_6$): $\delta$ 3.28 (t, 2H, $J = 6.6$ Hz), 3.64 (t, 2H, $J = 6.6$ Hz), 4.09 (brs, OH), 6.07 (s, 2H), 6.94 (s, 3H), 7.60 (brs, 2H, NH$_2$) ppm; $^{13}$C NMR (75.4 MHz, DMSO $d_6$): $\delta$ 32.05 (CH$_2$), 60.29 (CH$_2$), 86.03 (ArC), 94.41 (ArC), 101.99 (CH$_2$), 108.70 (ArCH), 108.94 (ArCH), 115.50 (CN), 115.64 (CN), 123.16 (ArCH), 127.51 (ArCH), 127.47 (ArCH), 147.90 (ArCH), 150.53 (ArC), 160.29 (ArC), 167.53 (ArC) ppm; HRMS: mass calculated for C$_{18}$H$_{12}$N$_4$O$_2$: 349.0583 (M + H) and 371.0400 (M + Na); Obs. mass: 349.0573 (M + H) and 371.0393 (M + Na).

2-Amino-4-(1,3-benzodioxol-5-yl)-6-[4-(methoxyphenyl)sulfanyl]-4-[4-(propan-2-yl)phenyl]pyridine-3,5-dicarbonitrile (7t): Solid; M.P. 224–226$^\circ$C; IR (KBr): 3348, 3235, 2220, 1650, 1541, 1479, 1251, 1084, 1036, 1020 cm$^{-1}$; $^1$H NMR (300 MHz, DMSO $d_6$): $\delta$ 3.28 (t, 2H, $J = 6.6$ Hz), 3.64 (t, 2H, $J = 6.6$ Hz), 4.09 (brs, OH), 6.07 (s, 2H), 6.94 (s, 3H), 7.60 (brs, 2H, NH$_2$) ppm; $^{13}$C NMR (75.4 MHz, DMSO $d_6$): $\delta$ 32.05 (CH$_2$), 60.29 (CH$_2$), 86.03 (ArC), 94.41 (ArC), 101.99 (CH$_2$), 108.70 (ArCH), 108.94 (ArCH), 115.50 (CN), 115.64 (CN), 123.16 (ArCH), 127.51 (ArCH), 127.47 (ArCH), 147.90 (ArCH), 150.53 (ArC), 160.29 (ArC), 167.53 (ArC) ppm; HRMS: mass calculated for C$_{18}$H$_{12}$N$_4$O$_2$: 349.0583 (M + H) and 371.0400 (M + Na); Obs. mass: 349.0573 (M + H) and 371.0393 (M + Na).

2-Amino-4-(1,3-benzodioxol-5-yl)-6-[4-(hydroxyethyl)phenyl]pyridine-3,5-dicarbonitrile (7u): Solid; M.P. 226–228$^\circ$C; IR (KBr): 3331, 3231, 2214, 1639, 1551, 1526, 1250, 1087, 1012 cm$^{-1}$; $^1$H NMR (300 MHz, DMSO $d_6$): $\delta$ 3.82 (s, 3H), 3.87 (s, 3H) 6.85 (d, 2H, $J = 7.9$ Hz), 7.05 (d, 2H, $J = 8.3$ Hz), 7.37–7.45 (bbrs, 2H, NH$_2$), 7.43–7.46 (brs, 4H) ppm; $^{13}$C NMR (75.4 MHz, DMSO $d_6$): $\delta$ 55.48 (OCH$_3$), 86.89 (ArC), 93.39 (ArC), 114.34 (ArCH), 115.11 (ArCH), 115.59 (CN), 117.94 (CN), 126.01 (ArC), 130.36 (ArCH), 137.23 (ArCH), 158.03 (ArCH), 160.19 (ArC), 160.90 (ArC), 161.32 (ArC), 168.19 (ArC) ppm; HRMS: mass calculated for C$_{21}$H$_{16}$N$_4$O$_2$: 389.1074 (M + H) and 411.0891 (M + Na); Obs. mass: 389.1064 (M + H) and 411.0884 (M + Na).
(M + H) and 363.0527 (M + Na); Obs. mass: 341.0701 (M + H) and 363.0519 (M + Na).

2-Amino-4-(1,3-benzodioxol-5-yl)-6-(benzylsulanyl)pyridine-3,5-dicarboxonitrile (7s): Solid; M.P. 226–228°C; IR (KBr): 3392, 3216, 2218, 1651, 1554, 1476, 1428, 1260, 1093, 1012 cm⁻¹; ¹H NMR (300 MHz, DMSO d₆): δ 4.42 (s, 2H), 6.04 (s, 2H), 6.91 (s, 3H), 7.25 (s, 3H), 7.40 (s, 2H), 7.67 (brs, 2H, NH₂) ppm; ¹³C NMR (75.4 MHz, DMSO d₆): δ 34.07 (CH₂), 82.70, 108.68 (ArCH), 108.96 (ArCH), 115.66 (CN), 123.16 (ArC), 124.10 (ArC), 127.63 (ArC), 130.41 (ArC) ppm; HRMS: mass calculated for C₂₁H₁₄N₄O₂S: 387.0908 (M + H) and 409.0734 (M + Na); Obs. mass: 387.0908 (M + H) and 409.0728 (M + Na).

2-Amino-4-(1,3-benzodioxol-5-yl)-6-(4-methylphenyl)sulfonylpyridine-3,5-dicarboxonitrile (7u): Solid; M.P. 256–258°C; IR (KBr): 3392, 3216, 2218, 1651, 1554, 1476, 1428, 1260, 1093, 1012 cm⁻¹; ¹H NMR (300 MHz, DMSO d₆): δ 2.37 (s, 3H), 6.14 (s, 2H), 7.05 (m, 3), 7.27 (m, 3H), 7.42 (d, 2H, J = 7.6 Hz), 7.61 (brs, 2H, NH₂) ppm; ¹³C NMR (75.4 MHz, DMSO d₆): δ 21.41 (CH₃), 87.33 (ArC), 93.76 (ArC), 102.20 (CH₂), 108.88 (ArCH), 109.11 (ArCH), 115.54 (CN), 123.34 (ArCH), 124.10 (ArC), 127.63 (ArC), 130.41 (ArCH), 130.88 (ArCH), 135.35 (ArCH), 147.88 (ArC), 149.50 (ArC), 160.16 (ArC) ppm; HRMS: mass calculated for C₂₁H₁₄N₄O₂S: 387.0917 (M + H) and 409.0734 (M + Na); Obs. mass: 387.0909 (M + H) and 409.0729 (M + Na).

2-amino-6-[2-aminophenyl]sulfonyl]-4-(furan-2-yl)pyridine-3,5-dicarboxonitrile (7v): Solid; M.P. 228°C; IR (KBr): 3392, 3216, 2218, 1651, 1554, 1476, 1428, 1260, 1093, 1012 cm⁻¹; ¹H NMR (300 MHz, DMSO d₆): δ 5.38 (s, 2H), 5.85 (t, 1H, J = 7.8 Hz), 6.82 (m, 2H), 7.24 (m, 2H), 7.38 (d, 1H, J = 3.6 Hz), 7.63 (brs, 2H, NH₂), 8.11 (s, 1H) ppm; ¹³C NMR (75.4 MHz, DMSO d₆): δ 82.70 (ArC), 90.32 (ArC), 108.09 (ArC), 113.23 (ArCH), 115.78 (ArCH), 116.09 (CN), 116.41 (CN), 116.61 (ArCH), 116.83 (ArCH), 132.13 (ArCH), 137.67 (ArCH), 144.41 (ArC), 145.65 (ArC), 146.90 (ArCH), 151.69 (ArC), 160.66 (ArC), 168.35 (ArC) ppm; HRMS: mass calculated for C₁₇H₁₄N₃OS: 334.0764 (M + H) and 356.0581 (M + Na); Obs. mass: 334.0757 (M + H) and 356.0575 (M + Na).

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