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ARTICLE TYPE

Desilylative activation of TMSCN in chemoselective Strecker-Ugi type reaction: Functional fused imidazoles as building blocks in an entry to annulated purines

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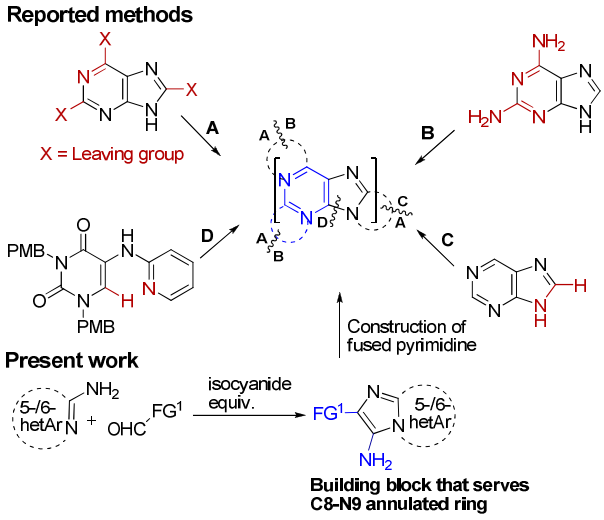
A pathway of desilylative activation of TMSCN as a functional isonitrile equivalent and DABCO-THF as an appropriate system for activation in a chemoselective Strecker-Ugi type reaction has rendered ethyl glyoxalate and various heterocyclic-2-amidines as feasible substrates, and afforded the successful synthesis of 3-amino-2-carboxyethyl substituted fused imidazoles to be useful as building blocks. This class of functional scaffold has provided via construction of fused pyrimidinone motif the synthesis of biologically important C8-N9 annulated purines, and adenines and their oxo/thio analogs. This new approach is convenient and flexible for preparation of versatile purine-condensed heterocycles.

Introduction

Purine class of compounds is known for their wide range of biological activities and use as valuable tools in chemical biology.[1] These properties have incited for the preparation of versatile derivatives and analogs of purines.[2] In this direction, the synthesis of annulated purines has recently gained importance. These compounds have been shown to posses various bioactivities[3] such as antihypertension, anti-inflammatory, human A3 adenosine receptor antagonism, and inhibition of PDE1/5 and tyrosine kinase EphB4. Furthermore, for some specific pharmacological activities, the purine derivatives have traditionally been considered as relatively less potent, while their analogs with an additional fused ring that represent a novel family of compounds have been reported to possess important activities, selectivities, physicochemical properties, and pharmacokinetic profiles.[3a-c,4] Various approaches are known for different kind of annulations at purines (Scheme 1). The frequently used approach for annulation (C6-N1/C8-N9) involves the double nucleophilic substitution reaction of leaving group-containing purine (path A).[3c-e,4,5] The approach requires additional reactions for incorporation of leaving group into purine. The method exploring the reaction of the amidine functionality in aminopurine for annulations is also known (path B). For example, the reaction of adenine, purine-2,6-diamine, or purine-8-amine with α-halocarbonyl constructs corresponding imidazole-fused purines.[6] Exploring the reactivity of amidine functionality, we developed also a multicomponent reaction of adenine or guanine with aldehyde and isocyanide towards preparation of aminoimidazole-fused compounds.[7] Hocek *et al* reported a methodology of intramolecular direct arene C-H arylation of suitably N9-aryl or arylalkyl substituted purines towards synthesis of purino[8,9-*f*]phenanthridines and 5,6-dihydropurino[8,9-*a*]isoquinolines (path C).[8] Recently, an approach involving Buchwald-Hartwig amination of *N*H-protected 5-halopyrimidine-2,4-dione with 2-aminopyridine, intramolecular C-H amination, and deprotection towards preparation of pyridine-fused purine-2,4-dione has been documented (path D).[9] Herein, we report the synthesis of suitably functionalized heterocyclic-condensed imidazole via an appropriate desilylative activation of TMSCN as a functional isonitrile equivalent in the Strecker-Ugi type reaction and exploration of heterocyclic-condensed imidazole as building block that affords access to heterocyclic-annulated purines (Scheme 1). While the literature-known methods for preparation of annulated purines involve mostly the construction of new



Scheme 1: Reported and present work

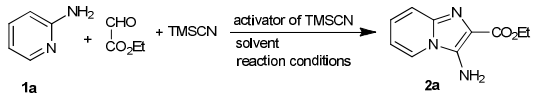
annulated ring starting from purine or the intramolecular building of imidazole ring, this present approach explores annulated ring-containing functional imidazole as an important building block. This approach can enable the preparation of purinones annulated at C8-N9 with various substituted 5/6-membered heteroaromatics which are not accessible by known methods.

Results and discussion

Synthesis of 3-amino-2-carboxyethyl substituted fused imidazoles

With our aim of establishing a new approach for synthesis of heterocyclic-annulated purine class of compounds, we were interested in exploring a suitably functionalized synthetic building block which could be prepared in one step. In this aspect, we considered N-fused imidazole with 2-carboxy ester and 3-amine functionalities, as the building block. The preparation of 3-amine and 2-aryl/alkyl substituted N-fused imidazoles involves the multicomponent reaction of heterocyclic-2-amidine and aldehyde with *iso*-octyl/*tert*-butyl isocyanide,[10] and subsequent de-*iso*-octylation[11] or de-*tert*-butylation.[12] Following these methods, we attempted the preparation of 3-amino-2-carboxyethylimidazo[1,2-*a*]-pyridine as a model building block by the reactions of 2-aminopyridine and ethyl glyoxalate with *iso*-octyl/*tert*-butyl isocyanide and follow up dealkylations promoted by TFA[11] or HBF_4[12], respectively. In these reactions, the desired product formed in low yields (24 and 27%, respectively), conversions were incomplete, and side reactions took place. The variation of solvent and reaction temperature in the process could not improve the yield of the product beyond 32%. Recently, we developed a Strecker-Ugi type reaction of heterocyclic-2-amidine and aldehyde with TMSCN as isocyanide equivalent in water, which afforded 3-amine and 2-aryl/alkyl substituted N-fused imidazoles in good yields.[13] Following this approach for the preparation of 3-amine and 2-carboxyethyl substituted imidazo[1,2-*a*]-pyridine, a reaction of ethyl glyoxalate and 2-aminopyridine with TMSCN was done. The product **2a** was obtained in 12% yield (entry 1, Table 1). Reaction was found to be incomplete and non-isolable side products also formed. We realized that several competing reactions were associated because of an additional functionality (α-ester) present in the aldehyde component, the amine substrate, and the product containing ester and amine functionalities. On the other hand, these groups in the product are required towards its function as a potential building block. For preparation of the building block, the approach using TMSCN as isocyanide equivalent compared to the MCR-dealkylation method is relatively step economical and was thus considered for exploration. We then investigated in our reaction some of the milder and efficient protocols reported for synthesis of α-aminonitrile via Strecker reaction using TMSCN. Rama Rao's approach[14] with β-cyclodextrin-catalysis or Kobayashi's conditions[15] using Et_3N for activation of TMSCN provided the product in trace and 10% yield only, respectively (entries 2 and 3). The combined use of a catalytic quantity of scandium triflate along with Et_3N in Kobayashi's conditions, which was known to promote the Strecker reaction for less reactive substrates, also resulted in poor reaction conversion and formation of several products (entry 4). Gratifyingly, a reaction using a tertiary amine that possess bi-nucleophilic sites, such as DABCO[16] in 1,4-dioxane provided significant improvement in yield of the product (entry 5). Microwave dielectric heating enhanced further the yield (entry 6). A survey of other ether solvents (entries 7-9), e.g., THF, DME, and Diglyme revealed their similar efficiency and THF was most effective. The reactions using DABCO in other different kind of solvents (entries 10-13), DMSO, MeCN, *n*-butanol, and polyethylene glycol indicated that these solvents were inferior compared to ether solvents. The reaction in THF was then investigated using various bases (entries 14-17) that could promote desilylation of TMSCN, such as DBU, triethylamine (TEA), diisopropylethylamine (DIPEA), and *N*-methylimidazole. DABCO was found to be most effective. One equivalent quantity of DABCO was found to be optimal.

Table 1: Optimization of the reaction[a]

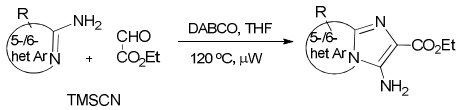


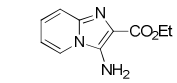
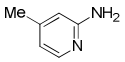
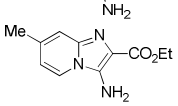
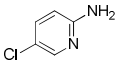
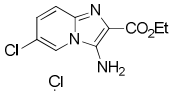
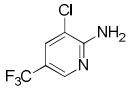
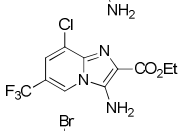
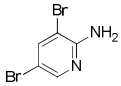
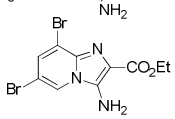
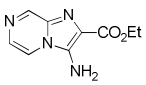
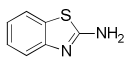
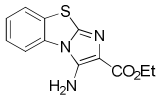
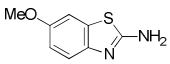
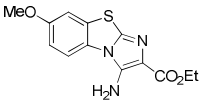
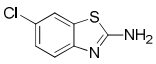
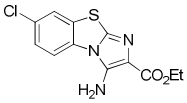
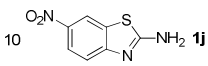
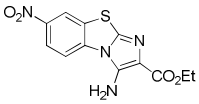
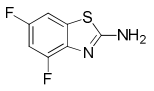
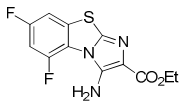
1a 2a

#	Activator[b]	Solvent	Reaction conditions[c]	Yield[d] (%)
1	KF	H_2O	RT, 5 h	12
2	β-Cyclodextrin	H_2O-MeOH[e]	RT, 24 h	traces
3	Et_3N	DCM	RT, 24 h	10
4	Et_3N-$Sc(OTf)_3$[f]	DCM	RT, 24 h	8
5	DABCO	1,4-dioxane	80 °C, 4h	50
6	DABCO	1,4-dioxane	μW, 120 °C, 30 min	58
7	DABCO	THF	μW, 120 °C, 15 min	70
8	DABCO	DME	μW, 120 °C, 15 min	62
9	DABCO	Diglyme	μW, 120 °C, 15 min	60
10	DABCO	DMSO	μW, 120 °C, 10 min	32
11	DABCO	MeCN	μW, 120 °C, 10 min	36
12	DABCO	*n*-butanol	μW, 120 °C, 10 min	17
13	DABCO	PEG-400	μW, 120 °C, 10 min	20
14	DBU	THF	μW, 120 °C, 30 min	22
15	TEA	THF	μW, 120 °C, 30 min	18
16	DIPEA	THF	μW, 120 °C, 30 min	15
17	*N*-methylimidazole	THF	μW, 120 °C, 30 min	20
18	DABCO-$Sc(OTf)_3$	THF	μW, 120 °C, 30 min	40
19	—	THF	μW, 120 °C, 30 min	5
20	$InCl_3$	THF	μW, 120 °C, 10 min	18
21	$Sc(OTf)_3$	THF	μW, 120 °C, 10 min	15

[a] 2-Aminopyridine (1 mmol), Ethyl glyoxalate (1 equiv.), TMSCN (1 equiv.); [b] Nucleophilic activator (1 equiv.) and Lewis acid (5 mol %) were used; [c] RT: Room temperature (25-27 °C), optimal reaction time for conventional oil bath heating or microwave irradiation; [d] isolated yield; [e] H_2O-MeOH (10:1); [f] Et_3N (1 equiv.)-$Sc(OTf)_3$ (20 mol%).

Table 2: Synthesis of various 3-amino-2-carboxyethyl-fused imidazoles[a]



#	amidine		product		yield (%)[b]
1		**1a**		**2a**	70
2		**1b**		**2b**	56
3		**1c**		**2c**	65
4		**1d**		**2d**	58
5		**1e**		**2e**	62
6		**1f**		**2f**	80
7		**1g**		**2g**	60
8		**1h**		**2h**	55
9		**1i**		**2i**	65
10		**1j**		**2j**	64
11		**1k**		**2k**	50

[a] N-heterocyclic amidines (1 mmol), Ethyl glyoxalate (1 equiv.), TMSCN (1 equiv.); [b] isolated yield.

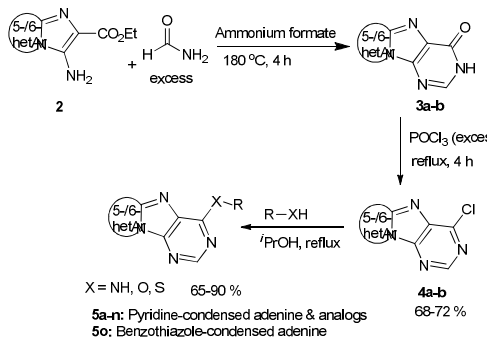
A reaction with combined use of DABCO and catalytic $Sc(OTf)_3$ resulted in several side reactions and inferior yield of product (entry 18). The reaction in absence of DABCO (entry 19) formed majorly imine with a little desired product. The Lewis acid-catalysis replacing DABCO in the reaction (entries 20 & 21) lowered the yield of the product. All these results of the optimization study indicate that the chemoselective Strecker-Ugi reaction using multifunctional substrate as in the present reaction crucially depends on nucleophilic activation pathway of TMSCN and DABCO-THF as an appropriate activators-system.

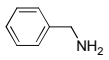
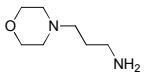
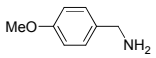
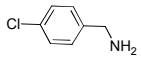
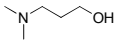
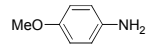
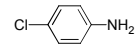
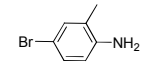
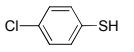
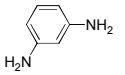
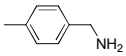
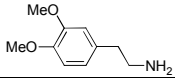
With the optimized protocol in hand, we next set out to explore its generality towards synthesis of 3-amine and 2-carboxyethyl functionalized various N-fused imidazoles. To our delight, versatile heterocyclic amidines including 2-aminopyridine, 2-aminopyrazine and 2-aminobenzothiazole with various substitutions underwent smooth reactions and provided functional N-fused imidazoles in good yields (Table 2). For Strecker-Ugi reaction using TMSCN, the present method has rendered for the first time ethyl glyoxalate as viable aldehyde substrate and flexibility for various heterocyclic-2-amidines including 2-aminobenzothiazole also. The electronic properties of the substituents in the heteroaromatic ring may change the nucleophilic behavior of amine in Strecker reaction and that of ring nitrogen atom in Ugi reaction. However, the electron-withdrawing groups (Br, Cl, F, CF_3, NO_2) and donating groups (Me, OMe) present in the heterocyclic-2-amidines did not have any significant disparity in the reaction. A strong electron-withdrawing group like NO_2 also at C6 of the benzothiazole did not diminish the yield of the product. The reaction conditions were found to be tolerant for chloro, bromo, methoxy and nitro functionalities, which provide the opportunity of their various further chemical manipulations in products.

Synthesis of heterocyclic-condensed adenines and their oxo/thio analogs

We then focused on exploring 3-amino-2-carboxyethylimidazo[1,2-*a*]pyridine (**2a**) as synthetic building block towards preparation of heterocyclic-enlarged adenines and their oxo/thio analogs (**5**, Table 3). Accordingly, a reaction of building block (**2a**) with formamide was investigated for the preparation of pyrido[1,2-*e*]purin-4(3*H*)-one (**3a**), precursor of compound **5**. The variation in equivalence of formamide, reaction temperature and mode of heating (conventional vs microwave irradiation) were evaluated. After several experiments, it was found that the reaction with formamide in excess quantity at 150 °C under microwave irradiation (2.5 h) provided product (**3a**) in 65% yield. Reaction at increased temperature, 170 °C for 2 h enhanced the yield of the product to 71%. In spite of good yield, the reaction required microwave irradiation for considerably longer time and yet was found to be incomplete. Therefore, we wanted to obtain a method using conventional heating. On the other hand, the reaction performed by conventional heating at 180 °C resulted in incomplete conversion and relatively low yield (46%). We then investigated the effect of ammonia source as additive in the reaction. Indeed, the use of ammonium formate (1 mol. equiv.) in the reaction under conventional heating (180 °C) afforded pyrido[1,2-*e*]purin-4(3*H*)-one (**3a**) in 82% yield. The subsequent deoxychlorination with $POCl_3$ gave 4-chloropyrido[1,2-*e*]purine (**4a**) in 72% yield. Aromatic nucleophilic substitution (S_NAr) of compound **4a** with an amine formed pyridine-annulated adenine (**5a**) in 90% yield (Table 3). In purine chemistry related to drug discovery and chemical biology research, the variation in amine/oxo/thio substitutions at 6-position of adenine is frequently followed.[17] Gratifyingly, the present new approach enabled the preparation of C8-N9-annulated adenines with diverse C4-amines and their oxo/thio-analogs (**5a-o**) in good yields. Anilines containing electron-donating as well as electron-withdrawing functionalities, sterically hindered aniline, benzyl amines, aliphatic amines, and the amines those are pharmaceutically important could be easily incorporated into the products. The reactions sequence

Table 3: Synthesis of pyridine-annulated adenines, and their oxo and thio analogs[a]



#	R−XH	Product	Yield (%) (step 3)[a]	#	R−XH	Product	Yield (%) (step 3)[b]
1		**5a**	90	9		**5i**	83
2		**5b**	87	10		**5j**	75
3		**5c**	85	11		**5k**	67
4		**5d**	88	12[c]		**5l**	70
5		**5e**	83	13		**5m**	83
6		**5f**	85	14		**5n**	82
7		**5g**	65	15		**5o**	78
8		**5h**	84				

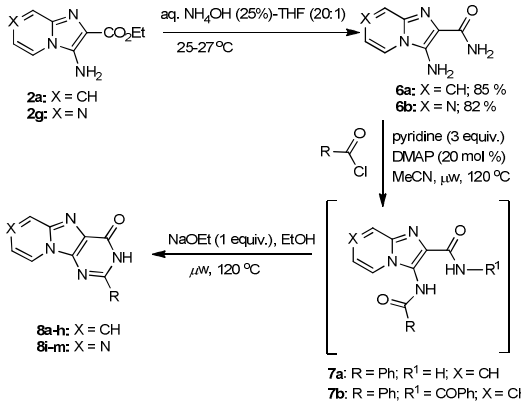
[a] The product (**3b**) formed in the reaction of compound **2g** with formamide could not be isolated in pure form due to its poor solubility and thus directly subjected to subsequent reaction after removal of excess formamide. [b] Isolated yield, [c] K_2CO_3 (1.5 equiv.) was utilized in S_NAr reaction (step 3).

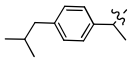
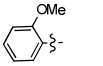
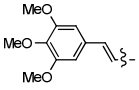
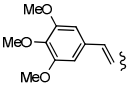
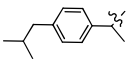
2→3→4→5 was also tried for other two representative 3-amino-2-carboxyethyl containing fused imidazoles **2**. Imidazo-fused benzothiazole **2g** The sequence worked well for and produced benzothiazole-condensed adenine **5o**. However, the product obtained in the reaction of imidazopyrazine **2f** with formamide could not be isolated because of its poor solubility.

Synthesis of 2-alkyl/aryl substituted heterocyclic-condensed purinones

In aspects of biological activities, the variation in 2-aryl/alkyl substitutions of the purine class of compounds is important.[18] Therefore, we were also interested in the preparation of various 2-aryl/alkyl substituted heterocyclic-enlarged purinones (**8**, Table 4) that could easily be converted into pyridine-enlarged adenines or their oxo/thio analogs by deoxychlorination and S_NAr-amination as described above. In this context, the reactions-sequence of transamidation of the building block 3-amino-2-carboxyethylimidazo[1,2-*a*]pyridine **2a**, *N*-aroylation of 3-amine, and amide-amide cyclo-condensation to construct pyrimidinone ring was considered (Scheme in Table 4). Keeping in mind the development of an operationally simple method, the transamidation of **2a** towards preparation of corresponding amide (**6a**) was performed by using aqueous ammonia solution. With 2 ml of 5% aq NH_4OH solution and THF (1 ml) for 1 mmol of **2a**, the reaction at room temperature was found to undergo a little conversion. The use of aqueous ammonia solution of increasing concentration and higher volume enhanced the reaction conversion and yield of the product. Increase in the relative volume of THF did not improve the yield. In the reaction using compound-25% aq NH_4OH-THF in 1 mmol : 20 ml : 1 ml, the best result (85% yield) was obtained. The use of methanolic ammonia replacing aqueous ammonia resulted in even slower reaction and formation of side products. The *N*-benzoylation of 3-amine functionality in compound **6a** using benzoyl chloride following classical methods caused chemoselectivity problem.

Table 4: Synthesis of 2-alkyl/aryl-pyrido[1,2-*e*]-purin-4(3*H*)-one



#	R	Product	Yield (%)[a]	#	R	Product	Yield (%)[a]
1		**8a**	44	8		**8h**	45
2		**8b**	24	9		**8i**	27
3		**8c**	32	10		**8j**	15
4		**8d**	30	11		**8k**	9
5		**8e**	37	12		**8l**	19
6		**8f**	40	13		**8m**	24
7		**8g**	42				

[a] Isolated yield.

The additional *N*-benzoylation of amide functionality as a competing reaction leading to formation of compound **7b** was also found to occur significantly. The optimal yield (62%) of *N*-benzoyl derivative of imidazopyridine-2-carboxamide-3-amine (**7a**) was obtained by using benzoyl chloride (1.4 equiv.), pyridine (3 equiv.), DMAP (20 mol %), MeCN as solvent, and microwave-assisted dielectric heating at 120 ºC. Interestingly, in

this reaction condition, the benzoylation of amide functionality was virtually eliminated. We then investigated the base-mediated intramolecular amide-amide cyclo-condensation of compound **7a** towards construction of pyridine-annulated purinone (**8a**). After several experiments, we found that use of NaOEt in EtOH under microwave irradiation provided the desired product (**8a**) in optimal yield (70 %), albeit the reaction was not complete. In this reaction condition, the compound **7a** also formed, although in small quantity (5 %), plausibly via alcoholysis of amide with ethoxide. Both N-benzoylation reaction and amide-amide cyclocondensation were performed in one pot avoiding intermediate chromatographic isolation, which provided the product in similar yield. The reactions sequence **2→6→7→8** was also tried for 3-amino-2-carboxyethyl containing imidazopyrazine **2f**, which afforded corresponding products **8i-m**. Following this developed reactions-route, various 2-aryl/alkyl substituted pyridine/pyrazine-enlarged purinones (**8a-m**, Table 4) were synthesized. The approach was flexible for incorporation of aryl, alkenyl and alkyl substitutions at C2 of products. The pharmacologically-relevant moieties, for example, 2-(4-isobutylphenyl)propyl (ibuprofen, anti-inflammatory drug), and trimethoxycinnamyl (anticancer agent) could be easily incorporated in the products.

Besides the literature-known common biological importance of annulated purine class of scaffolds, the pyridine C8-N9-fused purines (Table 3 and 4) represent also the structural amalgamation of purines with another scaffold, imidazo[1,2-*a*]pyridine[19] which possess a wide range of bio-activities[20] such as anticancer, antibacterial, antifungal, antiviral, anti-inflammatory agents, selective CDK inhibitors, GABA receptor agonists and calcium channel blockers. Imidazo[1,2-*a*]pyridine is also represented by marketed drugs, zolimidine and zolpidem. Therefore, these pyridine-condensed analogs of purine class of compounds are important for their potential versatile pharmacological activities.

Conclusion

In the present study, a one-step preparation of 3-amino and 2-carboxyethyl substituted fused imidazoles and use of this class of functional scaffold as synthetic building block for preparation of C8-N9 annulated purines have been explored. The Strecker-Ugi type reaction with TMSCN as a functional isonitrile equivalent by a desilylative activation pathway and DABCO-THF as an appropriate activators-system has rendered for the first time ethyl glyoxalate and various heterocyclic-2-amidines including 2-aminobenzothiazoles as feasible substrates and provides successful synthesis of the building blocks in good yields. Relevant substituted C8-N9 annulated purinones, and adenines and their oxo/thio analogs have been prepared from the building block via construction of fused pyrimidinone motif. This new approach can enable the convenient preparation of molecular diversity-feasible biologically important versatile C8-N9 annulated purines, and, therefore, has potential application in purine chemistry and drug discovery research.

Experimental section

General considerations: The starting materials and solvents were used as received from commercial sources without further purification. The ^{1}H and ^{13}C spectra were recorded in $CDCl_3$/DMSO-d_6/CD_3OD solvents on 400 MHz spectrometer using TMS as internal standard. HRMS was measured using TOF analyzer. Melting points determined are uncorrected. Microwave assisted reactions were carried out in sealed reaction vessel using Biotage Initiator.

Experimental procedure for synthesis of Ethyl 3-aminoimidazo[1,2-*a*]pyridine-2-carboxylate (2a, Table 1): A mixture of 2-aminopyridine (**1a**, 94 mg, 1 mmol) and ethyl glyoxalate solution (50% solution in toluene) (0.2 ml, 1 mmol) was stirred at RT (25-27 ºC) for 2 min. THF (2 ml) and DABCO (112 mg, 1 equiv.) were subsequently added. Reaction mixture was cooled to 0-5 ºC and TMSCN (0.125 ml, 1 mmol) was added. The mixture was heated under microwave irradiation at 120 °C. After completion of reaction (monitored by TLC, 15 min), solvent was evaporated under vacuum. The column chromatographic purification of crude mass on neutral alumina provided ethyl 3-aminoimidazo[1,2-*a*]pyridine-2-carboxylate (**2a**, 144 mg, 70%).

The other compounds (**2b-k**, Table 2) were prepared following this procedure.

Experimental procedure for synthesis of Pyrido[1,2-*e*]purin-4(3*H*)-one (3a, Table 3): Ethyl 3-aminoimidazo[1,2-*a*]pyridine-2-carboxylate (**2a**, 205 mg, 1 mmol) was taken in a round bottom flask. Formamide (2 ml) and ammonium formate (63 mg, 1 mmol) were added. The reaction mixture was heated at 180 °C. After completion of reaction (monitored by TLC, 4 h), the column chromatographic purification of crude mass on neutral alumina provided pyrido[1,2-*e*]purin-4(3*H*)-one (**3a**, 153 mg, 82%). The other compound (**3b**, Table 3) was prepared following this procedure.

Experimental procedure for synthesis of 4-Chloropyrido[1,2-*e*]purine (4a): Pyrido[1,2-*e*]purin-4(3*H*)-one (**3a**, 186 mg, 1 mmol) was taken in a round bottom flask under N_2. $POCl_3$ (2 ml) was added to it under a flow of N_2. Reaction mixture was heated at 120 °C. After completion of reaction (monitored by TLC, 4 h), the mixture was poured into ice-cold water. 20% Aqueous NaOH solution was added dropwise till pH 8. Then the solution was extracted with EtOAc (2 × 40 ml). The combined organic layer was washed with water (10 ml), dried with anhyd. Na_2SO_4, and concentrated under vacuum. The column chromatographic purification of crude mass on silica gel provided 4-chloropyrido[1,2-*e*]purine (**4a**, 147 mg, 72%). The other compound (**4b**, Table 3) was prepared following this procedure.

Representative experimental procedure for synthesis of *N*-Benzylpyrido[1,2-*e*]purin-4-amine (5a, Table 3, entry 1): To a solution of 4-chloropyrido[1,2-*e*]purine (**4a**, 204 mg, 1 mmol) in ^{i}PrOH (1 ml) in a round bottom flask, benzyl amine (128 mg, 1.2 mmol) was added. Reaction mixture was heated at 82 °C. After completion of the reaction (monitored by TLC, 2h), solvent was evaporated under vacuum. The column chromatographic purification of crude mass on neutral alumina provided *N*-benzylpyrido[1,2-*e*]purin-4-amine (**5a**, 248 mg, 90%).

The other compounds (**5b-o**, Table 3) were prepared following this procedure.

Experimental procedure for synthesis of 3-Aminoimidazo[1,2-*a*]pyridine-2-carboxamide (6a, Table 4): Ethyl 3-aminoimidazo[1,2-*a*]pyridine-2-carboxylate (**2a**, 2.05 g, 10 mmol) was taken in a round bottom flask. 25% Aqueous NH_4OH solution (200 ml) and THF (10 ml) were added and the mixture was stirred at RT (25-27 °C) under closed system. After maximum conversion (monitored by TLC, 7 days), solvents were evaporated under vacuum. The column chromatographic purification of crude mass on neutral alumina provided 3-aminoimidazo[1,2-*a*]pyridine-2-carboxamide (**6a**, 1.5 g, 85%). The other compound (**6b**, Table 4) was prepared following this procedure.

Representative experimental procedure for synthesis of 2-Phenylpyrido[1,2-*e*]purin-4(3*H*)-one (8a, Table 4, entry 1,): 3-Aminoimidazo[1,2-*a*]pyridine-2-carboxamide (**6a**, 177 mg, 1 mmol) was taken in a microwave vial under N_2. Acetonitrile (anhyd., 2 ml), DMAP (24.5 mg, 20 mol%), pyridine (0.25 ml, 3 mmol) and benzoyl chloride (196 mg, 1.4 mmol) were subsequently added to it under flow of N_2. Reation mixture was heated under microwave irradiation at 120 °C. After maximum conversion (monitored by TLC, 30 min.), solvent was evaporated under vacuum. The column chromatographic purification of crude mass on neutral alumina provided *N*-benzoylimidazo[1,2-*a*]pyridine-3-amine-2-carboxamide (**7a**, 174 mg, 62%). Then, to a solution of **7a** in anhydrous ethanol (1.5 ml) in a vial, sodium ethoxide (68 mg, 1 mmol) was added under flow of N_2 and the reaction mixture was heated at 120 °C under microwave irradiation. After completion of the reaction (monitored by TLC, 30 min.), solvent was evaporated under vacumn. The column chromatographic purification of crude mass on neutral alumina provided 2-phenylpyrido[1,2-*e*]purin-4(3*H*)-one (**8a**, 183 mg, 70%).

For products (**8b-m**, Table 4), the mixture obtained after *N*-benzoylation and removal of solvent without chromatographic isolation was directly subjected to the amide-amide cyclocondensation step.

1. Ethyl 3-aminoimidazo[1,2-*a*]pyridine-2-carboxylate (2a, Table 2, entry 1)[21]

Yellow green solid; mp >200 °C; 144 mg, 70% yield; IR (ATR) ν_{max} = 3419, 3084, 1681, 1109 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 8.19 (d, *J* = 7.0 Hz, 1H), 7.33 (d, *J* = 9.3 Hz, 1H), 7.07 (dd, *J* = 7.8 Hz, 7.9 Hz, 1H), 6.80 (dd, *J* = 6.8 Hz, 6.7 Hz, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 1.31 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, CD_3OD): δ = 164.9, 138.9, 137.9, 124.3, 123.7, 118.6, 113.1, 111.9, 59.7, 14.9; HRMS (ESI-TOF) Calcd for $C_{10}H_{11}N_3O_2Na$: $[M + Na]^+$ 228.0749 found m/z 228.0740.

2. Ethyl 3-amino-7-methylimidazo[1,2-*a*]pyridine-2-carboxylate (2b, Table 2, entry 2)

Yellow solid; mp >200 °C; 123 mg, 56% yield; IR (ATR) ν_{max} = 3436, 3132, 2988, 1701, 1616, 1207, 1105 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 8.09 (d, *J* = 7.1 Hz, 1H), 7.09 (s, 1H), 6.67 (d, *J* = 7.1 Hz, 1H), 6.31 (s, 2H) 4.27 (q, *J* = 7.0 Hz, 2H), 2.29 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 169.7, 143.5, 143.1, 139.5, 127.7, 120.9, 119.5, 117.4, 64.3, 26.1, 19.7; HRMS (ESI-TOF) Calcd for $C_{11}H_{14}N_3O_2$: $[M + H]^+$ 220.1088 found m/z 220.1083.

3. Ethyl 3-amino-6-chloroimidazo[1,2-*a*]pyridine-2-carboxylate (2c, Table 2, entry 3)

Green white solid; mp >200 °C; 156 mg, 65% yield; IR (ATR) ν_{max} = 3399, 2982, 1684, 1613, 1275, 1134, 1029, 782 cm^{-1}; ^1H NMR (400 MHz, CDCl3:DMSO-d_6): 8.37 (s, 1H), 7.31 (d, *J* = 9.7 Hz, 1H), 6.96 (dd, *J* = 9.7 Hz, 1.8 Hz, 1H), 6.22 (s, 2H), 4.37 (q, *J* = 7.0 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, CDCl3:DMSO-d_6): δ = 169.5, 143.5, 141.3, 130.0, 125.9, 124.5, 123.8, 119.1, 64.9, 19.4; HRMS (ESI-TOF) Calcd for $C_{10}H_{11}{}^{35}ClN_3O_2$: $[M + H]^+$ 240.0542 found m/z 240.0539 and for $C_{10}H_{11}{}^{37}ClN_3O_2$: $[M + H]^+$ 242.0512 found m/z 242.0511.

4. Ethyl 3-amino-8-chloro-6-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (2d, Table 2, entry 4)

Yellow solid; mp >200 °C; 179 mg, 58% yield; IR (ATR) ν_{max} = 3458, 3409, 3294, 2978, 1668, 1618, 1519, 1209, 1114 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): 8.95 (s, 1H), 7.54 (s, 1H), 6.82 (s, 2H), 4.32 (q, *J* = 7.0 Hz, 2H), 1.34 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 163.8, 141.1, 133.6, 124.0, 123.3 (q, $^1J_{C\text{-}F}$ = 270 Hz), 123.2 (q, $^3J_{C\text{-}F}$ = 5 Hz), 117.5, 113.9 (q, $^2J_{C\text{-}F}$ = 35 Hz), 113.6, 59.7, 14.5; HRMS (ESI-TOF) Calcd for $C_{11}H_{10}{}^{35}ClF_3N_3O_2$: $[M + H]^+$ 308.0415 found m/z 308.0425 and for $C_{11}H_{10}{}^{37}ClF_3N_3O_2$: $[M + H]^+$ 310.0386 found m/z 310.0396.

5. Ethyl 3-amino-6, 8-dibromoimidaz[1,2-*a*]pyridine-2-carboxylate (2e, Table 2, entry 5)

Yellow solid; mp >200 °C; 225 mg, 62% yield; IR (ATR) ν_{max} = 3473, 3286, 2980, 1677, 1629, 1260, 1214, 1150 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): 8.62 (s, 1H), 7.59 (s, 1H), 6.57 (s, 2H), 4.31 (q, *J* = 7.0 Hz, 2H), 1.33 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 164.3, 140.2, 134.1, 128.5, 123.6, 114.0, 112.9, 104.9, 60.1, 14.9; HRMS (ESI-TOF) Calcd for $C_{10}H_{10}{}^{79}Br_2N_3O_2$: $[M + H]^+$ 361.9142 found m/z 361.9141 and for $C_{10}H_{10}{}^{81}Br_2N_3O_2$: $[M + H]^+$ 363.9121 found m/z 363.9126.

6. Ethyl 3-aminoimidazo[1,2-*a*]pyrazine-2-carboxylate (2f, Table 2, entry 6)

Yellow solid; mp 180 °C; 165 mg, 80 % yield; IR (ATR) ν_{max} = 3452, 3292, 3245, 1703, 1622, 1189 cm^{-1}; ^1H NMR (400 MHz, CD_3OD): δ = 8.77 (d, *J* = 1.4 Hz, 1H), 8.08 (dd, *J* = 4.9 Hz, 1.4 Hz, 1H), 7.69 (d, *J* = 4.9 Hz, 1H), 4.42 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, CD_3OD): δ = 164.0, 144.4, 138.6, 133.4, 127.2, 115.9, 115.6, 60.4, 13.4; HRMS (ESI) Calcd for $C_9H_{10}N_4O_2Na$: $[M + Na]^+$ 229.0702 found m/z 229.0703.

7. Ethyl 3-aminobenzo[*d*]imidazo[2,1-*b*]thiazole-2-carboxylate (2g, Table 2, entry 7)

Pale white solid; mp >200 °C; 156 mg, 60% yield; IR (ATR) ν_{max} = 3401, 3296, 2979, 1663, 1617, 1211, 1115 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.71 (d, *J* = 7.9 Hz, 1H), 7.63 (dd, *J* = 0.9 Hz, 7.9 Hz, 1H), 7.41 (dt, *J* = 1.2 Hz, 8.0 Hz, 1H), 7.34 (dt, *J* = 1.2 Hz, 7.8 Hz, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.1, 143.5, 139.1, 131.7, 129.8, 126.6, 125.9, 125.2, 115.1, 114.3, 59.5, 14.9; HRMS (ESI-TOF) Calcd for $C_{12}H_{11}N_3O_2SNa$: $[M + Na]^+$ 284.0470 found m/z 284.0459.

8. Ethyl 3-amino-7-methoxybenzo[*d*]imidazo[2,1-*b*]thiazole-2-carboxylate (2h, Table 2, entry 8)

Yellow green solid; mp >200 °C; 160 mg, 55% yield; IR (ATR) ν_{max} = 3454, 3407, 3292, 2978, 1666, 1618, 1207, 1112 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): 8.03 (d, *J* = 8.9 Hz, 1H), 7.58 (d, *J* = 2.6 Hz, 1H), 7.06 (dd, *J* = 2.6 Hz, 8.9 Hz, 1H), 6.41 (s, 2H),

4.24 (q, J = 7.0 Hz, 2H), 3.82 (s, 3H), 1.29 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 164.1, 157.4, 143.1, 138.9, 131.4, 125.6, 114.89, 114.85, 113.2, 110.0, 59.5, 56.3, 14.9; HRMS (ESI-TOF) Calcd for $C_{13}H_{13}N_3O_3SNa$: $[M + Na]^+$ 314.0576 found m/z 314.0558.

9. Ethyl 3-amino-7-chlorobenzo[*d*]imidazo[2,1-*b*]thiazole-2-carboxylate (2i, Table 2, entry 9)

greenish white solid; mp >200 °C; 192 mg, 65% yield; IR (ATR) ν_{max} = 3402, 3282, 2978, 1666, 1617, 1212, 1118 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$:DMSO-d_6): 8.12 (d, J = 8.7 Hz, 1H), 7.83 (d, J = 1.6 Hz, 1H), 7.43 (dd, J = 2.0 Hz, 8.7 Hz, 1H), 6.40 (s, 2H), 4.31 (q, J = 7.1 Hz, 2H), 1.37 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$:DMSO-d_6): δ = 163.7, 142.9, 138.9, 131.6, 130.3, 130.1, 125.9, 123.9, 115.0, 114.8, 59.4, 14.5; HRMS (ESI-TOF) Calcd for $C_{12}H_{10}{}^{35}ClN_3O_2SNa$: $[M + Na]^+$ 318.0080 found m/z 318. 0073 and for $C_{12}H_{10}{}^{37}ClN_3O_2SNa$: $[M + Na]^+$ 320.0051 found m/z 320.0044.

10. Ethyl 3-amino-7-nitrobenzo[*d*]imidazo[2,1-*b*]thiazole-2-carboxylate (2j, Table 2, entry 10)

Yellow solid; mp >200 °C; 195 mg, 64% yield; IR (ATR) ν_{max} = 3454, 3401, 3290, 3111, 1683, 1619, 1520, 1340, 1277, 1148 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$:DMSO-d_6): 8.78 (d, J = 1.8 Hz, 1H), 8.33-8.32 (m, 2H), 6.54 (s, 2H), 4.33 (q, J = 7.1 Hz, 2H), 1.37 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$:DMSO-d_6): δ = 163.6, 144.3, 143.0, 139.3, 135.6, 131.4, 121.6, 120.1, 115.3, 113.8, 59.4, 14.3; HRMS (ESI-TOF) Calcd for $C_{12}H_{11}N_4O_4S$: $[M + H]^+$ 307.0503 found m/z 307.0496.

11. Ethyl 3-amino-5,7-difluorobenzo[*d*]imidazo[2,1-*b*]thiazole-2-carboxylate (2k, Table 2, entry 11)

Yellow green solid; mp 185-187 °C; 148 mg, 50% yield; IR (ATR) ν_{max} = 3461, 3294, 2987, 1676, 1646, 1317, 1118 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.21 (d, J = 5.9 Hz, 1H), 7.03-6.97 (m, 1H), 5.84 (s, 2H), 4.39 (q, J = 7.1 Hz, 2H), 1.43 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.0, 159.4 (d, $^1J_{C\text{-}F}$ = 236 Hz), 148.6 (d, $^1J_{C\text{-}F}$ = 236 Hz), 142.1, 138.2, 133.9 (d, $^2J_{C\text{-}F}$ = 13 Hz), 114.7, 107.7 (d, $^2J_{C\text{-}F}$ = 21 Hz), 102.3 (dd, $^2J_{C\text{-}F}$ = 28 Hz, 23 Hz), 59.9, 14.4; HRMS (ESI-TOF) Calcd for $C_{12}H_9F_2N_3O_2SNa$: $[M + Na]^+$ 320.0282 found m/z 320.0287.

12. Pyrido[1,2-*e*]purin-4(3*H*)-one (3a)[22]

White solid; mp >200 °C; 152 mg, 82% yield; IR (ATR) ν_{max} = 3422, 3092, 3042, 1682, 1578 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.67 (td, J = 1.2 Hz, 6.9 Hz, 1H), 8.16 (s, 1H), 7.70 (td, J = 1.0 Hz, 9.3 Hz, 1H), 7.56-7.52 (m, 1H), 7.11 (dt, J = 1.1 Hz, 6.8 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 157.8, 144.3, 143.9, 141.4, 129.3, 126.7, 124.5, 118.2, 113.1; HRMS (ESI-TOF) Calcd for $C_9H_7N_4O$ $[M+H]^+$ 187.0622 Found *m/z* 187.0614.

13. 4-Chloropyrido[1,2-*e*]purine (4a)[22]

White solid; mp >200 °C; 147 mg, 72% yield; IR (ATR) ν_{max} = 3012, 2923, 1395 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.88 (s, 1H), 8.77 (d, J = 6.8 Hz, 1H), 7.82 (d, J = 9.4 Hz, 1H), 7.70-7.66 (m, 1H), 7.09 (t, J = 6.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.0, 149.2, 149.1, 146.3, 133.3, 132.8, 125.2, 119.1, 112.8; HRMS (ESI-TOF) Calcd for $C_9H_5ClN_4Na$: $[M + Na]^+$ 227.0101 found m/z 227.0101.

14. 4-chlorobenzo[4,5]thiazolo[3,2-*e*]purine (4b)

White solid; mp >200 °C; 177 mg, 68% yield; IR (ATR) ν_{max} = 3038, 2850, 1694, 750 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.84 (s, 1H), 8.48 (d, J = 8.1 Hz, 1H), 7.79 (d, J = 8.0 Hz, 1H), 7.63 (dd, J = 7.6 Hz, 7.9 Hz, 1H), 7.51 (dd, J = 7.6 Hz, 7.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ =158.2, 150.2, 148.8, 148.6, 136.1, 131.2, 128.9, 127.6, 126.5, 124.2, 115.2; HRMS (ESI-TOF) Calcd for $C_{11}H_6ClN_4S$: $[M + H]^+$ 261.0003 found m/z 260.9996.

15. *N*-Benzylpyrido[1,2-*e*]purin-4-amine (5a, Table 3, entry 1)

White solid; mp 163-165 °C; 248 mg, 90% yield; IR (ATR) ν_{max} = 3251, 2850, 1615, 1314 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.58 (d, J = 6.9 Hz, 1H), 8.52 (s, 1H), 7.55 (d, J = 9.3 Hz, 1H), 7.43-7.38 (m, 1H), 7.31 (d, J = 6.2 Hz, 2H), 7.28-7.22 (m, 3H), 6.92-6.89 (m, 2H), 4.87 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ =155.2, 151.3, 145.6, 138.1, 129.9, 128.5, 127.7, 127.4, 124.4, 121.8, 118.2, 111.7, 44.7; HRMS (ESI-TOF) calcd for $C_{16}H_{13}N_5Na$: $[M + Na]^+$ 298.1069, found m/z 298.1070.

16. *N*-(4-Methoxybenzyl)pyrido[1,2-*e*]purin-4-amine (5b, Table 3, entry 2)

White solid; mp 160-162 °C; 265 mg, 87% yield; IR (ATR) ν_{max} = 3320, 2922, 1606, 1316 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.59 (d, J = 6.9 Hz, 1H), 8.53 (s, 1H), 7.58 (d, J = 9.3 Hz, 1H), 7.44-7.40 (m, 1H), 7.28 (d, J = 8.6 Hz, 2H), 6.92 (dd, J = 6.7 Hz, 6.8 Hz, 1H), 6.82 (d, J = 8.6 Hz, 2H), 6.71 (brs, NH), 4.81 (s, 2H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.0, 155.1, 151.3, 145.5, 130.2, 129.9, 129.1, 124.5, 121.7, 118.2, 113.9, 111.8, 55.3, 44.3; HRMS (ESI-TOF) calcd for $C_{17}H_{15}N_5ONa$: $[M + Na]^+$ 328.1175, found m/z 328.1172.

17. *N*-(4-Chlorobenzyl)pyrido[1,2-*e*]purin-4-amine (5c, Table 3, entry 3)

White solid; mp 165-167 °C; 262 mg, 85% yield; IR (ATR) ν_{max} = 3316, 2922, 1608, 1318, cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.61 (d, J = 6.9 Hz, 1H), 8.52 (s, 1H), 7.56 (d, J = 9.3 Hz, 1H), 7.45-7.41 (m, 1H), 7.25 (d, J = 8.8 Hz, 2H), 7.21 (d, 8.8 Hz, 2H), 6.93 (t, J = 6.5 Hz, 1H), 6.88 (s, NH), 4.85 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.1, 151.2, 145.7, 136.8, 133.2, 130.0, 128.9, 128.7, 124.5, 121.8, 118.2, 111.8, 43.9; HRMS (ESI-TOF) Calcd for $C_{16}H_{13}{}^{35}ClN_5$ $[M+H]^+$ 310.0861 Found *m/z* 310.0856.

18. *N*-(4-Methoxyphenyl)pyrido[1,2-*e*]purin-4-amine (5d, Table 3, entry 4)

White solid; mp 125-127 °C; 256 mg, 88% yield; IR (ATR) ν_{max} = 3280, 3045, 1640, 1614, 1509, 1319 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.65 (d, J = 6.4 Hz, 1H), 8.6 (s, 1H), 8.08-8.03 (m, 1H), 7.75 (d, J = 8.2 Hz, 1H), 7.65 (d, J = 8.9 Hz, 1H), 7.51-7.47 (m, 1H), 6.97-6.95 (m, 3H), 3.84 (S, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ =156.3, 152.9, 150.9, 145.9, 143.5, 131.5, 130.3, 124.5, 122.4, 122.2, 118.2, 114.3, 111.9, 55.6; HRMS (ESI-TOF) calcd for $C_{16}H_{13}N_5ONa$: $[M + Na]^+$ 314.1018, found m/z 314.1012.

19. *N*-(4'-Chlorophenyl)pyrido[1,2-*e*]purin-4-amine (5e, Table 3, entry 5)

White solid; mp >200 °C; 245 mg, 83% yield; IR (ATR) ν_{max} = 3396, 3320, 2921, 1618, 1578, 1316 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.68-8.65 (m, 2H), 8.04 (s, NH), 7.87 (d, J = 8.6 Hz, 2H), 7.67 (d, J = 9.3 Hz, 1H), 7.55-7.51 (m, 1H), 7.37 (d, J = 8.6 Hz, 2H), 7.00 (t, J = 6.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.3, 150.6, 146.3, 143.8, 137.3, 130.7, 129.1, 128.5, 124.6, 121.3, 118.3, 112.1; HRMS (ESI-TOF) calcd for $C_{15}H_{10}{}^{35}ClN_5Na$: $[M + Na]^+$ 318.0523 found m/z 318.0530.

20. *N*-(4'-Bromo-2'-methylphenyl)pyrido[1,2-*e*]purin-4-amine

(5f, Table 3, entry 6)

White solid; mp 193-195 °C; 300 mg, 85% yield; IR (neat) ν_{max} = 3416, 2921, 1578, 1311, 1113 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.66 (d, *J* = 6.9 Hz, 1H), 8.60 (s, 1H), 8.09 (d, *J* = 9.2 Hz, 1H), 7.68 (d, *J* = 9.2 Hz, 2H), 7.54-7.50 (m, 1H), 7.43-7.42 (m, 2H), 6.99 (dd, *J* = 6.8 Hz, 6.7 Hz, 1H) 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.9, 150.7, 146.3, 143.9, 135.4, 133.4, 132.1, 130.6, 129.7, 124.7, 124.6, 122.5, 118.3, 117.7, 112.0, 17.9; HRMS (ESI-TOF) calcd for $C_{16}H_{12}Br^{79}N_5Na$: $[M + Na]^+$ 376.0174 found m/z 376.0175 and for $C_{16}H_{12}{}^{79}Br^{81}N_5Na$: $[M + Na]^+$ 378.0154 found m/z 378.0153

21. *N*-(3'-anilino)pyrido[1,2-*e*]purin-4-amine (5g, Table 3, entry 7)

White solid; mp >200 °C; 179 mg, 65% yield; IR (ATR) ν_{max} = 3325, 3216, 1574, 1479, 1315 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 9.85 (s, 1H), 8.78 (d, *J* = 6.8 Hz, 1H), 8.5 (s, NH), 7.74 (d, *J* = 9.3 Hz, 1H), 7.65-7.61 (m, 1H), 7.34 (s, NH_2), 7.13-7.09 (m, 2H), 6.99(t, *J* = 7.9 Hz, 1H), 6.32 (d, *J* = 7.7 Hz, 1H), 5.06 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 153.1, 150.6, 149.3, 145.6, 143.7, 140.4, 131.3, 129.2, 125.3, 122.4, 118.2, 112.8, 109.8, 109.6, 107.0; HRMS (ESI-TOF) calcd for $C_{15}H_{12}N_6Na$: $[M + Na]^+$ 299.1021 found m/z 299.1027.

22. *N*-(3',4'-dimethoxyphenethyl)pyrido[1,2-*e*]purin-4-amine (5h, Table 3, entry 8)

White solid; mp 157-159 °C; 293 mg, 84% yield; IR (ATR) ν_{max} = 3220, 2923, 1597, 1317 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.60 (d, *J* = 6.7 Hz, 1H), 8.52 (s, 1H), 7.60 (d, *J* = 9.2 Hz, 1H), 7.45-7.41 (m, 1H), 6.92 (t, *J* = 6.6 Hz, 1H), 6.81-6.78 (m, 3H), 6.28 (brs, NH), 3.97 (brs, 2H), 3.86 (s, 3H), 3.85 (s, 3H), 2.98 (t, *J* = 6.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.4, 151.3, 149.0, 147.7, 145.5, 131.3, 129.8, 124.5, 121.9, 120.7, 118.2, 112.0, 111.7, 111.4, 55.9, 55.8, 42.1, 35.4 ; HRMS (ESI-TOF) calcd for $C_{19}H_{19}N_5O_2Na$: $[M + Na]^+$ 372.1437, found m/z 372.1435.

23. *N*-(3'-Morpholinopropyl)pyrido[1,2-*e*]purin-4-amine (5i, Table 3, entry 9)

White solid; mp 105-107 °C; 259 mg, 83% yield; IR (ATR) ν_{max} = 3301, 2946, 1617, 1316, 1112 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.58 (d, *J* = 6.9 Hz, 1H), 8.46 (s, 1H), 7.60 (d, *J* = 9.3 Hz, 1H), 7.43-7.39 (m, 2H), 6.90 (t, *J* = 6.7 Hz, 1H), 3.84-3.79 (m, 6H), 2.56 (t, *J* = 6.5 Hz, 2H), 2.50 (s, 4H), 1.94-1.87 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.5, 151.3, 145.4, 129.5, 124.4, 122.0, 118.3, 111.1, 66.9, 57.4, 53.8, 40.3, 25.3; HRMS (ESI-TOF) calcd for $C_{16}H_{20}N_6ONa$: $[M + Na]^+$ 335.1597 found m/z 335.1609.

24. *N*-Allylpyrido[1,2-*e*]purin-4-amine (5j, Table 3, entry 10)

White solid; mp 157-159 °C; 169 mg, 75 % yield; IR (ATR) ν_{max} = 3212, 3045, 1638, 1586, 1316 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.61(d, *J* = 6.9 Hz, 1H), 8.51 (s, 1H), 7.62 (d, *J* = 9.3 Hz, 1H), 7.45 (dd, *J* = 9.3 Hz, 6.6 Hz, 1H), 6.93 (dd, *J* = 6.6 Hz, 6.8 Hz, 1H), 6.38 (s, NH) 6.08-5.98(m, 1H) 5.32 (d, *J* = 17.1 Hz, 1H), 5.19 (d, *J* =10.3 Hz, 1H), 4.36 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.2, 151.2, 145.6, 134.0, 129.9, 124.5, 121.8, 118.3, 116.6, 111.8, 43.1; HRMS (ESI-TOF) Calcd for $C_{12}H_{12}N_5$ $[M+H]^+$ 226.1094 Found *m/z* 226.1086.

25. 4-(3'-*N*,*N*-Dimethylpropyloxy)pyrido[1,2-*e*]purine (5k, Table 3, entry 11)

White solid; mp 85-87 °C; 181 mg, 67% yield; IR (neat) ν_{max} = 3354, 1591, 1321 cm^{-1}; ^1H NMR (400 MHz, CD_3OD): δ = 8.78 (dt, J_1 = 6.9 Hz, J_2 = 1.1 Hz, 1H), 8.58 (s, 1H), 7.71-7.69 (m, 2H), 7.17-7.14 (m, 1H), 4.71 (t, *J* = 6.3 Hz, 2H), 2.71-2.67 (m, 2H), 2.35 (s, 6H) 2.17-2.13 (m, 2H); ^{13}C NMR (100 MHz, CD_3OD): δ = 160.8, 149.5, 147.2, 145.9, 132.4, 124.7, 122.2, 117.3, 112.7, 65.4, 55.7, 43.9, 26.2; HRMS (ESI-TOF) calcd for $C_{14}H_{17}N_5ONa$: $[M + Na]^+$ 294.1331 found m/z 294.1331.

26. 4-Phenoxypyrido[1,2-*e*]purine (5l, Table 3, entry 12)

White solid; mp 140-142 °C; 183 mg, 70% yield; IR (ATR) ν_{max} = 3120, 2921, 1557, 1307 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.72 (d, *J* = 6.6 Hz, 1H), 8.61 (s, 1H), 7.79 (d, *J* = 9.2 Hz, 1H), 7.60-7.56 (m, 1H), 7.51-7.47 (m, 2H), 7.36-7.31 (m, 3H), 7.03 (t, *J* = 6.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.7, 152.4, 149.6, 147.8, 147.2, 131.6, 129.7, 125.9, 124.7, 123.6, 121.9, 119.1, 112.3, ; HRMS (ESI-TOF) calcd for $C_{15}H_{10}N_4ONa$: $[M + Na]^+$ 285.0746 found m/z 285.0746.

27. 4-(Phenylthio)pyrido[1,2-*e*]purine (5m, Table 3, entry 13)

White solid; mp 158-160 °C; 230 mg, 83% yield; IR (ATR) ν_{max} = 3033, 1567, 1557, 1391, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.73 (s, 1H), 8.70 (d, *J* = 6.9 Hz, 1H), 7.79 (d, *J* = 9.3 Hz, 1H), 7.74-7.72 (m, 2H), 7.61-7.57 (m, 1H), 7.52-7.50 (m, 3H), 7.01 (dd, *J* = 6.7 Hz, 6.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.3, 149.9, 147.7, 143.1, 135.6, 132.0, 131.8, 129.7, 129.4, 127.1, 124.9, 118.9, 112.3; HRMS (ESI-TOF) calcd for $C_{15}H_{10}N_4SNa$: $[M + Na]^+$ 301.0524 found m/z 301.0529.

28. 4-((4'-Chlorophenyl)thio)pyrido[1,2-*e*]purine (5n, Table 3, entry 14)

White solid; mp >200 °C; 256 mg, 82% yield; IR (ATR) ν_{max} = 3041, 1562, 1384 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.72 (s, 1H), 8.70 (d, *J* = 6.9 Hz, 1H), 7.79 (d, *J* = 9.4 Hz, 1H), 7.64 (d, *J* = 8.5 Hz, 2H), 7.61-7.57 (m, 1H), 7.46 (d, *J* = 6.5 Hz, 2H), 7.01 (dd, *J* = 6.8 Hz, 6.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.6, 149.8, 147.8, 143.3, 136.8, 136.1, 132.1, 131.9, 129.6, 125.7 , 124.9, 118.9, 112.3; HRMS (ESI-TOF) calcd for $C_{15}H_9ClN_4SNa$: $[M + Na]^+$ 335.0134 found m/z 335.0133.

29. *N*-(4-methylbenzyl)benzo[4,5]thiazolo[3,2-*e*]purin-4-amine (5o, Table 3, entry 15)

White solid; mp >200 °C; 269 mg, 78% yield; IR (ATR) ν_{max} = 3188, 2970, 1594 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.50 (s, 1H), 8.42 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 7.9 Hz, 1H), 7.55 (dd *J* = 8.0 Hz, 7.6 Hz, 1H), 7.41 (dd *J*= 7.9 Hz, 7.6 Hz, 1H), 7.26 (d, *J* = 7.9 Hz, 2H), 7.11 (d, *J* = 7.8 Hz, 2H), 6.14 (s, NH), 4.85 (s, 2H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.6, 151.8, 151.7, 137.2, 135.2, 131.9, 129.3, 129.1, 127.7, 126.9, 125.5, 124.2, 123.9, 114.9, 44.6, 21.1; HRMS (ESI-TOF) calcd for $C_{19}H_{16}N_5S$: $[M + H]^+$ 346.1128 found m/z 346.1142.

30. 3-Aminoimidazo[1,2-*a*]pyridine-2-carboxamide (6a)[23]

White solid; mp 154-156 °C; 150 mg, 85% yield; IR (ATR) ν_{max} = 3308, 1655, 1601 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 8.11 (d, *J* = 7.0 Hz, 1H), 7.34-7.31 (m, 2H), 7.08-7.03 (m, 2H), 6.79 (dd *J* = 6.8 Hz, 6.7 Hz, 1H), 6.12 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 166.9, 136.6, 135.3, 123.1, 122.9, 117.5, 116.1, 111.2; HRMS (ESI-TOF) Calcd for $C_8H_8N_4ONa$: $[M + Na]^+$ 199.0596 found m/z 199.0590.

31. 3-Aminoimidazo[1,2-*a*]pyrazine-2-carboxamide (6b)

Yellow solid; mp 180 °C; 145 mg, 82 % yield; IR (ATR) ν_{max} = 3438, 3376, 3285, 3206, 1664, 1638, 1590, 1241 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 8.79 (s, 1H), 8.17-8.14 (m,1H), 7.69-

7.66 (m, 1H), 7.58 (s, 1H), 7.28 (s, 1H) 6.45 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 166.3, 144.1, 135.9, 132.1, 127.4, 118.2, 115.8; HRMS (ESI) Calcd for $C_7H_7N_5ONa$: $[M + Na]^+$ 200.0549 found m/z 200.0543.

32. 3-Benzamidoimidazo[1,2-*a*]pyridine-2-carboxamide (7a)

White solid; mp >200 °C; 174 mg, 62% yield; IR (neat) ν_{max} = 3298, 3229, 1684, 1663, 1601 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.04 (s, 1H), 8.14 (d, *J* = 7.1 Hz, 1H), 8.06 (d, *J* = 7.2 Hz, 2H), 7.63-7.59 (m, 2H), 7.57-7.51 (m, 3H), 7.33-7.28 (m, 1H), 6.91 (t, *J* = 6.9 Hz, 1H), 6.19 (s,1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 166.6, 166.1, 141.3, 132.8, 132.6, 128.9, 127.9, 126.7, 126.3, 125.3, 125.1, 117.8, 112.8; HRMS (ESI-TOF) calcd for $C_{15}H_{12}N_4O_2Na$: $[M+Na]^+$ 303.0858, found m/z 303.0884.

33. 3-Benzamido-*N*-benzoylimidazo[1,2-*a*]pyridine-2-carboxamide (7b)

White solid; mp >200 °C; IR (neat) ν_{max} = 3325, 1728, 1672, 1582, 1458 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.61 (s, 1H), 9.77 (s, 1H), 8.21 (d, *J* = 7.0 Hz, 1H), 8.11 (d, *J* = 7.3 Hz, 2H), 8.03 (d, *J* = 7.3 Hz, 2H), 7.67-7.54 (m, 7H), 7.37-7.33 (m, 1H), 6.96 (t, *J* = 6.6 Hz, 1H),; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 166.1, 164.7, 162.3, 141.3, 133.2, 133.0, 132.3, 129.0, 128.9, 127.9, 127.8, 126.9, 126.7, 126.4, 124.9, 118.3, 113.2; HRMS (ESI-TOF) calcd for $C_{22}H_{16}N_4O_3$: $[M+Na]^+$ 407.1120, found m/z 407.1126.

34. 2-Phenyl-3*H*-pyrido[1,2-*e*]purin-4-one (8a, Table 4, entry 1)

White solid; mp 110-112 °C; 115 mg, 44% yield; IR (neat) ν_{max} = 3496, 3299, 1661, 1640, 1582 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.31 (d, *J* = 6.9 Hz, 1H), 8.10 (d, *J* = 7.6 Hz, 2H), 7.72-7.69 (m, 2H), 7.62 (dd, *J* = 7.4 Hz, 7.5 Hz, 2H), 7.52 (dd, *J* = 7.0 Hz, 8.8 Hz, 1H), 7.14 (t, *J* = 6.8 Hz, 1H),; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 166.1, 142.6, 132.8, 132.1, 128.7, 128.1, 127.9, 126.9, 124.9, 117.7, 114.5, 114.2, 111.6; HRMS (ESI-TOF) calcd for $C_{15}H_{10}N_4ONa$: $[M+Na]^+$ 285.0753, found m/z 285.0745.

35. 2-(4-Chlorophenyl)-3*H*-pyrido[1,2-*e*]purin-4-one (8b, Table 4, entry 2)

Light yellow solid; mp >200 °C; 71 mg, 24% yield; IR (neat) ν_{max} = 3344, 2922, 1678, 1635, 1588 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.76 (d, *J* = 6.7 Hz, 1H), 8.27 (d, *J* = 8.4 Hz, 2H), 7. 71 (d, *J* = 9.2 Hz, 1H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.56-7.52 (m, 1H), 7.12 (t, *J* = 6.7 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 170.4, 141.9, 135.9, 132.4, 132.2, 128.6, 128.2, 125.3, 123.9, 116.8, 115.8, 112.2; HRMS (ESI-TOF) calcd for $C_{15}H_9ClN_4ONa$: $[M+Na]^+$ 319.0363, found m/z 319.0364.

36. 2-(2'-Methoxyphenyl)-3*H*-pyrido[1,2-*e*]purin-4-one (8c, Table 4, entry 3)

White solid; mp 185-187 °C; 94 mg, 32% yield; IR (neat) ν_{max} = 3396, 3297, 1674, 1238 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.68 (dt, *J* = 6.9 Hz, 1.1 Hz, 1H), 7.81 (dd, J_1 = 7.6, J_2 = 1.8 Hz, 1H), 7.69 (d, *J* = 9.3 Hz, 1H), 7.55-7.49 (m, 2H), 7.20 (d, *J* = 8.2 Hz, 1H), 7.13-7.06 (m, 2H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 157.9, 157.0, 150.9, 144.6, 141.9, 132.2, 130.5, 129.2, 125.2, 124.5, 122.1, 120.5, 118.2, 112.9, 111.9, 55.8; HRMS (ESI-TOF) calcd for $C_{16}H_{12}N_4O_2Na$: $[M + Na]^+$ 315.0858, found m/z 315.0854.

37. (*E*)-2-Phenethenyl-3*H*-pyrido[1,2-*e*]purin-4-one (8d, Table 4, entry 4)

Yellow solid; mp >200 °C; 86 mg, 30% yield; IR (neat) ν_{max} = 3411, 2919, 2850, 1706, 1615, 1579 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.68 (d, *J* = 6.7 Hz, 1H), 7.95 (d, *J* = 16 Hz, 1H), 7.69-7.63 (m, 3H), 7.51-7.40 (m, 4H), 7.12-7.08 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ =158.6, 150.8, 145.2, 142.4, 138.2, 135.4, 130.2, 129.8, 129.6, 127.9, 125.9, 124.9, 120.7, 118.8, 113.6; HRMS (ESI-TOF) calcd for $C_{17}H_{12}N_4ONa$: $[M+Na]^+$ 311.0909, found m/z 311.0901.

38. (*E*)-2-(3',4',5'-Trimethoxyphenethenyl)-3*H*-pyrido[1,2-*e*]purin-4-one (8e, Table 4, entry 5)

Yellow solid; mp >200 °C; 140 mg, 37% yield; IR (neat) ν_{max} = 2988, 1692, 1587, 1127 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$ + CD_3OD): δ = 8.62 (d, *J* = 6.8 Hz, 1H), 7.89 (d, *J* = 15.9 Hz, 1H), 7.66 (d, *J* = 9.2 Hz, 1H), 7.50-7.47 (m, 1H), 7.06-7.03 (m, 1H), 6.92(d, *J* = 16 Hz, 1H), 6.88 (s, 2H), 3.93 (s, 6H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$ + CD_3OD): δ = 162.9, 157.3, 154.7, 149.8, 146.7, 143.4, 143.0, 134.8, 133.8, 129.0, 128.2, 122.6, 122.3, 117.2, 108.8, 64.8, 59.9; HRMS (ESI-TOF) calcd for $C_{20}H_{18}N_4O_4Na$: $[M+Na]^+$ 401.1226, found m/z 401.1220.

39. 2-Benzyl-3*H*-pyrido[1,2-*e*]purin-4-one (8f, Table 4, entry 6)

White solid; mp >200 °C; 110 mg, 40% yield; IR (neat) ν_{max} = 3356, 3083, 1670, 1588 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.57 (d, *J* = 6.8 Hz, 1H), 7.66 (d, *J* = 9.3 Hz, 1H), 7.49-7.46 (m, 1H), 7.39 (d, *J* = 7.3 Hz, 2H), 7.32 (dd, *J* = 7.2 Hz, 7.6 Hz, 2H), 7.25-7.22 (m, 1H), 7.04 (dd, *J* = 6.6 Hz, 6.5 Hz, 1H), 4.07 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.7, 155.5, 144.8, 142.2, 137.1, 129.5, 129.2, 129.0, 127.3, 125.4, 124.8, 118.7, 113.5, 44.8; HRMS (ESI-TOF) calcd for $C_{16}H_{12}N_4ONa$: $[M + Na]^+$ 299.0909, found m/z 299.0901.

40. 2-(2'-(Pyridin-3''-yl)ethyl)-3*H*-pyrido[1,2-*e*]purin-4-one (8g, Table 4, entry 7)

Light yellow solid; mp >200 °C; 122 mg, 42% yield; IR (neat) ν_{max} = 3449, 3038, 2920, 1703, 1682 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.62 (d, *J* = 6.8 Hz, 2H), 8.51 (s, 1H), 8.40 (d, *J* = 4.0 Hz, 1H), 7.72-7.67 (m, 2H), 7.52-7.48 (m, 1H), 7.31 (dd, J_1 = 4.8, J_2 = 2.8 Hz, 1H), 7.08 (dd, *J* = 6.8 Hz, 6.6 Hz, 1H), 3.15-3.11 (m, 2H), 3.07-3.04 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.7, 155.9, 150.2, 147.9, 144.8, 142.1, 136.5, 129.5, 125.4, 124.8, 123.9, 118.7, 113.5, 35.7, 30.2; MS (APCI) m/z: 357 (MH^+), HRMS (ESI-TOF) calcd for $C_{16}H_{13}N_5ONa$: $[M + Na]^+$ 314.1018, found m/z 314.1011.

41. 2-(1'-(4''-(2'''-methylpropyl)phenyl)ethyl)-3*H*-pyrido[1,2-*e*]purin-4-one (8h, Table 4, entry 8)

White solid; mp 190-192 °C; 156 mg, 45% yield; IR (neat) ν_{max} = 3421, 2925, 1667, 1583 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.63 (dt, *J* = 6.9 Hz, 1.0 Hz, 1H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.50-7.46 (m, 1H), 7.30 (d, *J* = 8.1 Hz, 2H), 7.09-7.05 (m, 3H), 4.22 (q, *J* = 7.1, 1H), 2.36 (d, *J* = 7.1 Hz, 2H), 1.76-1.73 (m, 1H), 1.64 (d, *J* = 7.1 Hz, 3H), 0.80 (d, *J* = 6.6 Hz, 6H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.9, 158.7, 144.9, 142.1, 140.20, 140.17, 129.5, 127.5, 125.4, 124.8, 118.7, 113.5, 44.6, 43.3, 30.0, 22.6, 20.0; HRMS (ESI-TOF) calcd for $C_{21}H_{21}N_4ONa$: $[M+Na]^+$ 369.1692, found m/z 369.1685.

42. 2-Phenyl-3*H*-pyrazino[2,1-*e*]purin-4-one (8i, Table 4, entry 9)

White solid; mp >200 °C; 71 mg, 27% yield; IR (neat) ν_{max} = 3408, 1668 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.35 (s, 1H), 9.00 (d, *J* = 3.4 Hz, 1H), 8.26 (d, *J* = 4.2 Hz, 1H), 8.19 (d, *J*

= 7.1 Hz, 2H), 7.62-7.56 (m, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.7, 156.8, 156.4, 143.4, 142.1, 133.3, 132.1, 131.1 (2CH), 129.2 (2CH), 128.6, 121.1, 108.9; HRMS (ESI) calcd for $C_{14}H_9N_5ONa$: $[M + Na]^+$ 286.0705, found m/z 286.0695.

43. 2-(2-Methoxyphenyl)-3*H*-pyrazino[2,1-*e*]purin-4-one (8j, Table 4, entry 10)

Light yellow solid; mp >200 °C; 44 mg, 15% yield; IR (neat) ν_{max} = 3445, 3243, 2922, 1712, 1646, 1241, 1015 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.29 (s, 1H), 8.71 (d, J = 3.4 Hz, 1H), 8.04 (d, J = 4.6 Hz, 1H), 7.79 (dd J = 7.6 Hz, 1.5 Hz, 1H), 7.59-7.55 (m, 1H), 7.23 (d, J = 8.4 Hz, 1H), 7.13 (dd, J = 7.6 Hz, 7.5 Hz, 1H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.3, 157.6, 152.9, 146.4, 141.9, 139.5, 133.1, 131.1, 129.5, 126.7, 122.1, 121.0, 118.1, 112.5, 56.4; HRMS (ESI) calcd for $C_{15}H_{11}N_5O_2Na$: $[M+Na]^+$ 316.0811, found m/z 316.0820.

44. (*E*)-2-Styryl-3*H*-pyrazino[2,1-*e*]purin-4-one (8k, Table 4, entry 11)

Yellow solid; mp >200 °C; 26 mg, 9% yield; IR (neat) ν_{max} = 3411, 2919, 2850, 1706, 1579, 1125 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.20 (s,1H), 8.65 (d, J = 4.6 Hz, 1H), 8.02 (d, J = 4.6 Hz, 1H), 7.96 (d, J = 16.0 Hz, 1H), 7.64 (d, J = 6.9 Hz, 2H), 7.46-7.40 (m, 3H), 7.06 (d, J = 16.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.8, 152.5, 146.2, 142.1, 139.55, 139.50, 135.1, 130.5, 129.6 (2CH), 129.4, 128.2 (2CH), 126.7, 120.1, 117.9; HRMS (ESI) calcd for $C_{16}H_{11}N_5ONa$: $[M+Na]^+$ 312.0862, found m/z 312.0861.

45. (*E*)-2-(3,4,5-Trimethoxystyryl)-3*H*-pyrazino[2,1-*e*]purin-4-one (8l, Table 4, entry 12)

Yellow solid; mp >200 °C; 72 mg, 19% yield; IR (neat) ν_{max} = 3415, 2921, 1727, 1680, 1285, 1124 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.25 (d, J = 1.3 Hz, 1H), 8.62 (dd, J_1 = 4.6, J_2 = 1.4 Hz, 1H), 8.05 (d, J = 4.6 Hz, 1H), 7.93 (d, J = 16.0 Hz, 1H), 7.06 (d, J = 16.0 Hz, 1H), 6.97 (s, 2H) 3.84 (s, 6H), 3.70 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.2, 153.1 (2C), 152.3, 152.1, 145.9, 141.7, 139.1, 139.0, 130.4, 129.1, 129.0, 119.2, 117.3, 105.0 (2CH), 60.1, 55.9 ($2CH_3$); HRMS (ESI) calcd for $C_{19}H_{17}N_5O_4Na$: $[M+Na]^+$ 402.1179, found m/z 402.1175.

46. 2-(1-(4-Isobutylphenyl)ethyl)-3*H*-pyrazino[2,1-*e*]purin-4-one (8m, Table 4, entry 13)

White solid; mp >200 °C; 83 mg, 24% yield; IR (neat) ν_{max} = 3385, 2919, 1670 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.25 (s, 1H), 8.68 (d, J = 6.8 Hz, 1H), 8.03 (d, J = 4.2 Hz, 1H), 7.32 (d, J = 7.4 Hz, 2H), 7.10 (d, J = 7.4 Hz, 2H), 2.39 (d, J = 6.5 Hz, 2H), 1.79-1.76 (m, 1H), 1.66 (d, J = 6.6 Hz, 3H), 0.83 (d, J = 6.2 Hz, 6H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 160.8, 158.9, 146.4, 141.8, 140.3, 139.9, 139.3, 129.6 (2CH), 129.4, 127.6 (2CH), 126.5, 117.9, 44.6, 43.5, 30.0, 22.6 ($2CH_3$), 20.0; HRMS (ESI) calcd for $C_{20}H_{21}N_5ONa$: $[M+Na]^+$ 370.1644, found m/z 370.1643

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