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Cascade reaction synthesis of multisubstituted bicyclic pyridone derivatives

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ABSTRACT

An efficient synthesis of novel bicyclic pyridone derivatives via cascade reaction of heterocyclic ketene aminals (HKAs) and 4-arylmethylene-2-phenyloxazol-5(4*H*)-ones in the presence of acetic acid has been established. Significantly, the protocol affords a straightforward approach to the construction of multi-substituted bicyclic pyridones in which one C–O bond was cleaved and new C–C and C–N bonds were formed in one pot under mild conditions.

1. Introduction

Pyridone scaffolds are ubiquitous in a large number of natural products and biologically active molecules.[1] Among them, substituted bicyclic pyridones possess a broad range of pharmacological activities, including CB_2 agonists,[2] (the inhibitors of aldosterone synthase,[3] Amyloidβ-peptide aggregation,[4] irreversible 3CP,[5] pilus formation in uropathogenic *Escherichia coli*,[6,7] ACE (A58365A & A58365B, Fig. 1)).[8] Especially, which have antibacterial (ABT-719)[9] anticancer[10] and anti-HIV activities.[11] Hence, the synthesis of bicyclic pyridones has become a valuable strategy for discovering new bioactive compounds. Synthetic strategies that enable an efficient and rapid preparation of these interesting scaffolds are necessary.

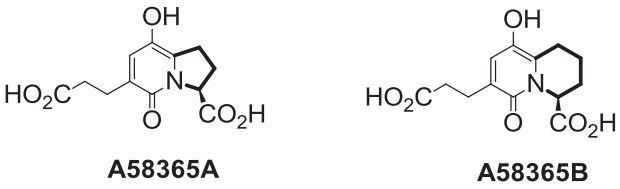

Fig. 1. Biologically active bicyclic pyridones.

To meet these demands, considerable attention has been paid to cascade reactions.[12] Cascade reactions proceed through multiple steps in one pot and include multiple bond formations. This is a promising strategy for the rapid and efficient construction of functionalised architectures.[13] Cascade reactions are powerful tools in combinatorial chemistry as well as diversity-oriented synthesis,[14] and have been utilized in the construction of diverse chemical libraries of heterocyclic compounds.[15] Those compounds could provide applications in modern drug discovery and development processes. Therefore, it is necessary to develop some novel cascade reactions that could achieve the construction of diverse combinatorial compound libraries.

Heterocyclic ketene aminals (HKAs) have been proven to be the important building blocks in the construction of heterocyclic systems,[16] especially the condensed heterocyclic compounds[17] through cascade or multi-component reactions.[16,17] Reactions of HKAs with a variety of α,β-unsaturated compounds via aza-ene reaction have been widely applied for the creation of diverse heterocycles in recent years. However, such aza-ene reaction via the cascade approach is scarcely reported.

Nowadays, many substrates, such as propiolic ester,[18] diethyl but-2-ynedioate[19] β-ketoesterenol tosylates[20] and other biselectrophiles[21] have been used as the building block to cyclocondense with heterocyclic ketene aminals to construct bicyclic pyridones. But these methods usually only get the simple compounds with poor diversity. This, in turn, places limitations on the flexibility and subsequent applications of this chemistry. It is

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of great importance to explore novel synthetic methods to meet the above-mentioned demands.

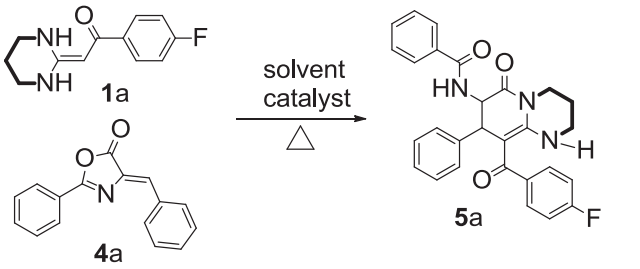
Built upon our progressive endeavours in exploring novel cascade reactions to synthesize highly substitute heterocyclic compounds, we herein reported a novel and efficient protocol for the synthesis of a new series of highly substituted bicyclic pyridone derivatives via a cascade reaction of HKAs & 4-arylmethylene-2-phenyloxazol-5(4*H*)-ones.

2. Result and discussion

Our approach toward the design and development of new cascade procedures involved the use of HKAs **1**–**3** and 4-arylmethylene-2-phenyloxazol-5(4*H*)-ones **4** that contain a number of chemically distinct functionalities, which could rapidly generate diverse bicyclic pyridone compounds. The starting material 4-arylmethylene-2-phenyloxazol-5-(4*H*)-ones **4** was easily obtained by the reaction of aldehyde and hippuric acid at 110 °C in the presence of sodium acetate in the solvent of acetic anhydride.[22] Building block HKAs were not commercially available, and were prepared according to reported procedures.[23]

Firstly, we used HKAs **1a** and 4-benzylidene-2-phenyloxazol-5(4*H*)-one **4a** as a simple substrates template to optimize reaction conditions. Different organic solvents, such as dioxane, ethanol and DMF were tested to synthesis of **5a** in the presence of various inexpensive and available catalysts at reflux (Table 1).

Table 1
Optimisation of the reaction conditions



Entry	Solvent	Catalyst (mol %)	*t* (°C)	Time (h)	Yield (%)[a]
1	EtOH	—	rt	72	n.r.
2	EtOH	—	Reflux	72	n.r.
3	Dioxane	—	Reflux	72	n.r.
4	Dioxane	Et_3N (20%)	Reflux	72	n.r.
5	EtOH	Piperidine (20%)	Reflux	72	n.r.
6	DMF	HOAc (20%)	110 °C	2	72
7	Dioxane	HOAc (20%)	Reflux	2	36
8	EtOH	HOAc (20%)	Reflux	2	81
9	DMF	TFA (20%)	110 °C	2	27
10	Dioxane	TFA (20%)	Reflux	2	12
11	EtOH	TFA (20%)	Reflux	2	Trace
12	EtOH	*p*-TSA(20%)	Reflux	2	12
13	DMF	*p*-TSA (20%)	110 °C	2	13
14	Dioxane	*p*-TSA (20%)	Reflux	2	12
15	EtOH	HOAc (30%)	Reflux	2	90
16	EtOH	HOAc (40%)	Reflux	2	81
17	EtOH	HOAc (50%)	Reflux	2	69

[a] Isolated yields based on HKA**1a**. n.r.=no reaction.

The results showed that no transformation occurred in the presence of basic catalysts or without catalyst between room temperature and the reflux temperatures in different solvents, even with a period of 72 h (Table 1, entries 1–5). Nevertheless, when acetic acid was added to the DMF, ethanol or dioxane, the reaction was proceeded by heat, with the yield of **5a** reaching 36% and 81% (Table 1, entries 6–8), respectively. Previous results have revealed that (i) acid is favoured in this cascade reaction; and (ii) ethanol was proven to be the best solvent. Based on these results, we continued to optimise reaction conditions to further improve the chemical yield. Subsequently, different acidic catalysts (20 mol %) were employed for this cascade reaction (Table 1, entries 9–14). Results showed that the whole series of acidic catalysts could promote the reaction smoothly, while acetic acid proved to be the best (Table 1, entries 8–14). Next, the amount of acetic acid was screened; the results showed that a concentration of 30 mol % was the best (Table 1, entry 15). Therefore, the reaction conditions of 30 mol % acetic acid as a catalyst at reflux in EtOH were found to be optimal for the preparation of **5a**.

Under the optimum conditions, we obtained different functionalised bicyclic pyridones by this method. To our delight, a series of *N*-(9-benzoyl-6-oxo-8-phenyl-2,3,4,6,7,8-hexahydro-1*H*-pyrido[1,2-*a*]pyrimidin-7-yl)-benzamides **5** was obtained in good yields (Table 2).

To further expand the scope of applications of this cascade reaction and to enlarge the library of bicyclic pyridones, different substituents in the aryl groups of the starting 4-aryliene-2-phenyloxazol-5(4*H*)-ones, including indole (Table 2, entries 22–26), furan (Table 2, entries 14–21), and thiophene (Table 2, entries 9–13) groups, were examined. The successful production of pyrido[1,2-*a*]pyrimidine derivatives indicated that this cascade reaction was general for such transformations.

It is worth noting that the HKAs with electron-withdrawing substituents (Table 2, entries 20–21) gave higher yields than those with electron-donating substituents. However, the electronic nature of the aryl group in the substituent **4** has a slightly impact on the reaction yield (Table 2, entries 2 vs 6, 10 vs23). A substrate with a more electron-donating aryl afforded a much lower yield than a similar substrate with a less electron-rich aryl. We reasoned that an electron-rich aryl group can decrease the electrophilicity of the C=C bond, which reduces nucleophilic attack of the double bond.

In order to further explore the scopes and limitations of this protocol, the subtrate 4-arylmethylene-2-phenyloxazol-5-(4*H*)-ones **4** were changed to other aryl group with fluorine and methyl substituents (Scheme 1). Corresponding products **5** were obtained. The results revealed that 4-arylmethylene-2-phenyloxazol-5-(4*H*)-ones, with various substituents, were all good substrates for the cascade reaction.

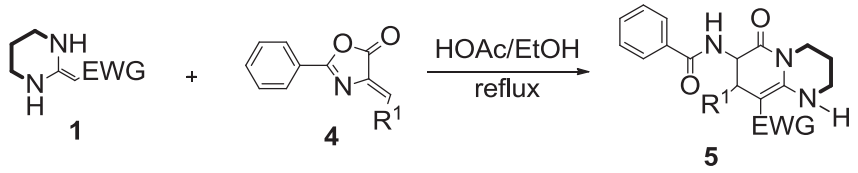
Subsequently, the substrate of HKAs **1** was also extended by using other five-membered HKAs **2** & the seven-member HKA **3**, and was reacted with 4-arylmethylene-2-phenyloxazol-5- (4*H*)-ones **4** (Table 3 & Scheme 2). The reactions proceed smoothly under the same conditions and we got the final product with moderate to good yields.

The size of heterocycles of heterocyclic ketene aminals also has a significant impact on the reaction. Generally, six-membered HKAs often give higher yields than five-membered ones, for example, the yield of **6c** was only 73% (Table 3, entries 3), whereas the yield of the six-membered **5x** was 75% (Table 2, entries 24).

All new compounds **5**–**7** were fully characterized on the basis of ^1H NMR, ^{13}C NMR spectra and high resolution mass spectra. The structure of product **5a** was further confirmed by X-ray crystallographic analysis[24] CCDC 953332 (Fig. 2).

A proposed mechanism of the HOAc-catalysed cascade reaction is described in Scheme 3. First, the carbonyl of 4-arylmethylene-2-phenyloxazol-5(4*H*)-ones **4** accepts one proton to give the intermediate **8**. The strong electron-withdrawing keto-carbonyl groups at the α-position of the HKA and the electron-donating diamino groups of HKA, HKA **1**–**3** serve as a heteroene component to react with α,β-unsaturated compound **8** to form compounds **9** via Michael addition reaction. Then an imine–enamine tautomerization[21f] was followed to produce**10**. Then, the NH group of intermediate **10** attacks the intramolecular carbonyl group via a cyclisation reaction to form **11**. Finally, hemiacetal **11** furnishes the product **5**–**7** via ring cleavage & enol–keto tautomerism.

Table 2
Cascade reaction synthesis of products **5** from various of **1** and **4**



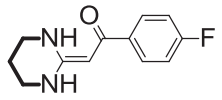
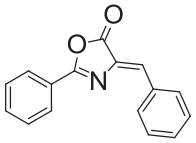
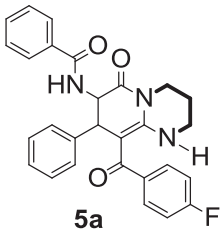
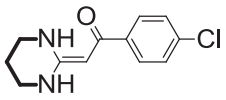
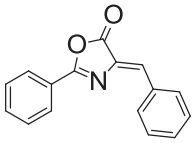
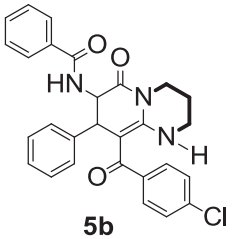
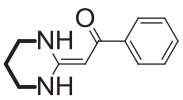
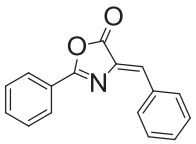
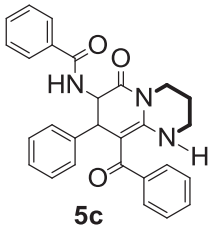
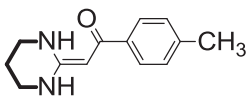
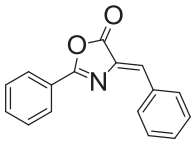
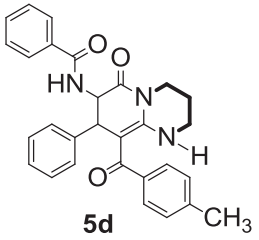
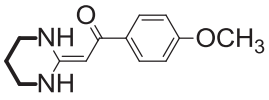
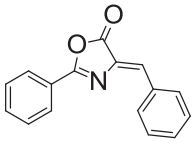
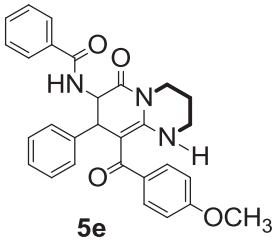
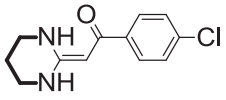
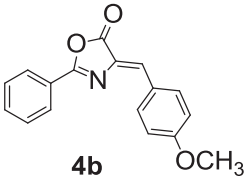
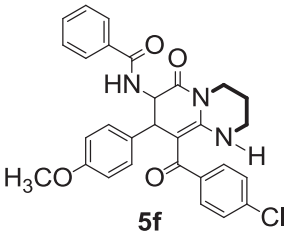
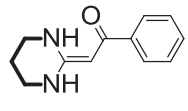
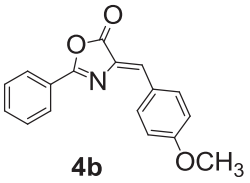
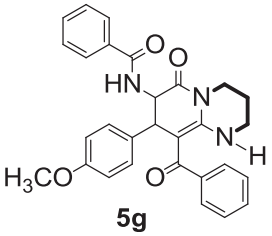
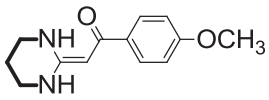
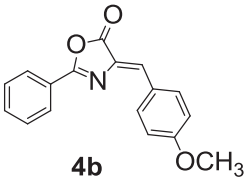
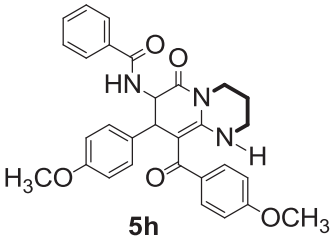
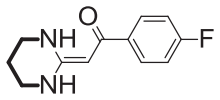
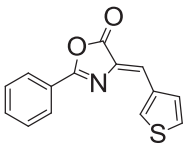
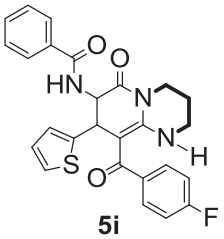
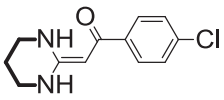
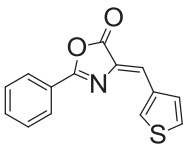
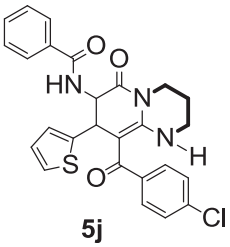
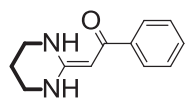
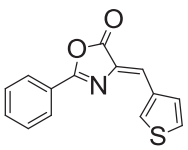
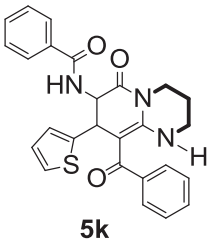
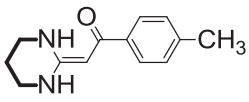
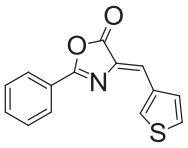
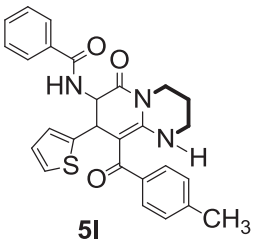
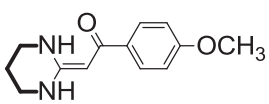
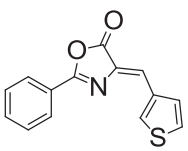
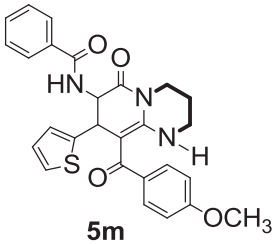
Entry	1	4	5	Yield (%)[a]
1	 **1a**	 **4a**	 **5a**	90
2	 **1b**	 **4a**	 **5b**	88
3	 **1c**	 **4a**	 **5c**	85
4	 **1d**	 **4a**	 **5d**	84
5	 **1e**	 **4a**	 **5e**	84
6	 **1b**	 **4b**	 **5f**	82

Table 2 (*continued*)

Entry	1	4	5	Yield (%)[a]
7	 **1c**	 **4b**	 **5g**	82
8	 **1e**	 **4b**	 **5h**	80
9	 **1a**	 **4c**	 **5i**	79
10	 **1b**	 **4c**	 **5j**	79
11	 **1c**	 **4c**	 **5k**	80
12	 **1d**	 **4c**	 **5l**	79
13	 **1e**	 **4c**	 **5m**	79

(*continued on next page*)

Table 2 (*continued*)

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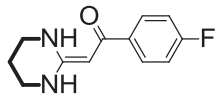
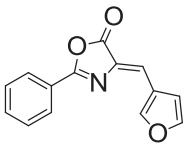
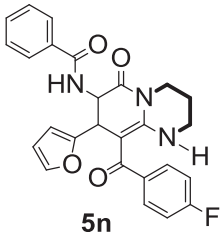
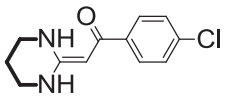
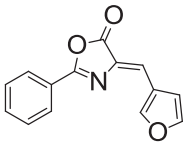
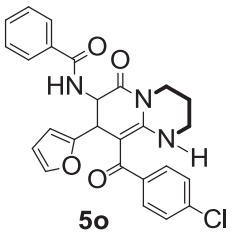
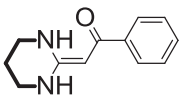
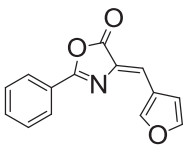
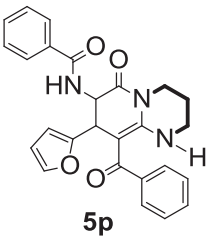
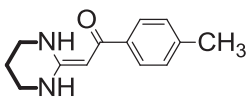
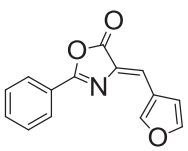
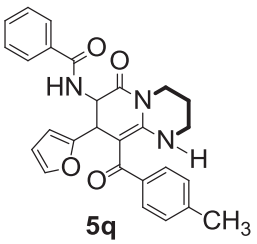
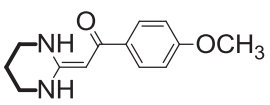
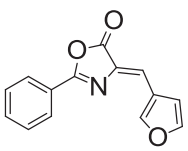
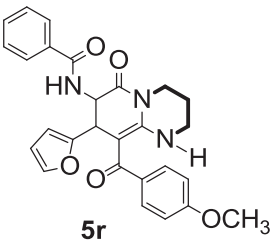
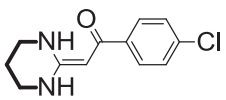
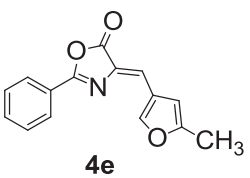
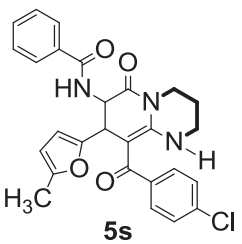
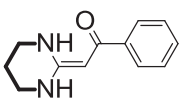
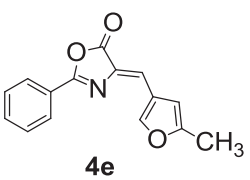
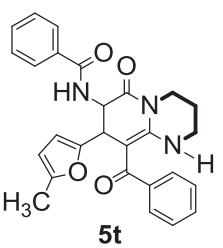
14	 **1a**	 **4d**	 **5n**	79
15	 **1b**	 **4d**	 **5o**	80
16	 **1c**	 **4d**	 **5p**	80
17	 **1d**	 **4d**	 **5q**	79
18	 **1e**	 **4d**	 **5r**	76
19	 **1b**	 **4e**	 **5s**	79
20	 **1c**	 **4e**	 **5t**	77

Table 2 (*continued*)

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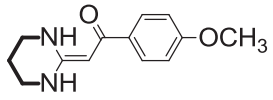
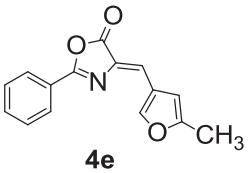
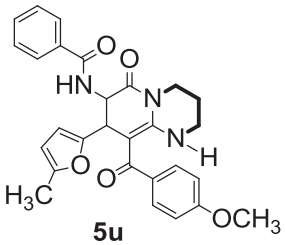
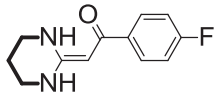
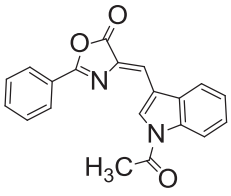
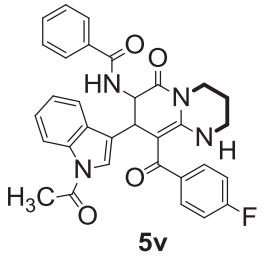
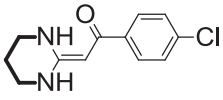
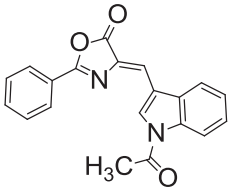
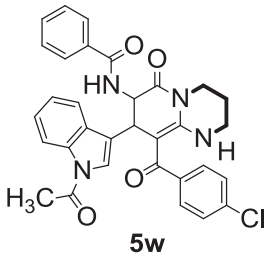
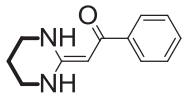
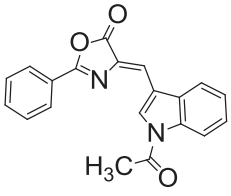
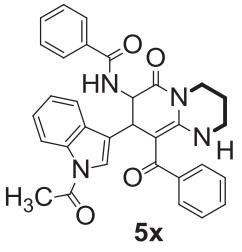
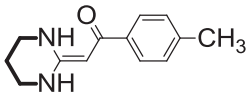
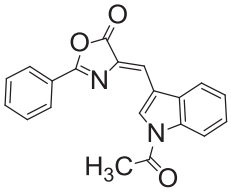
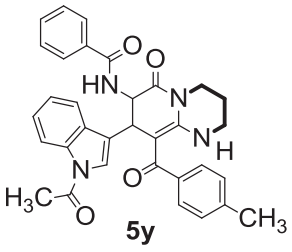
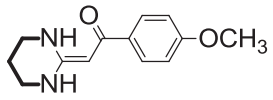
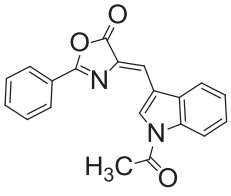
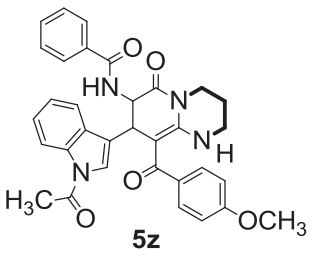
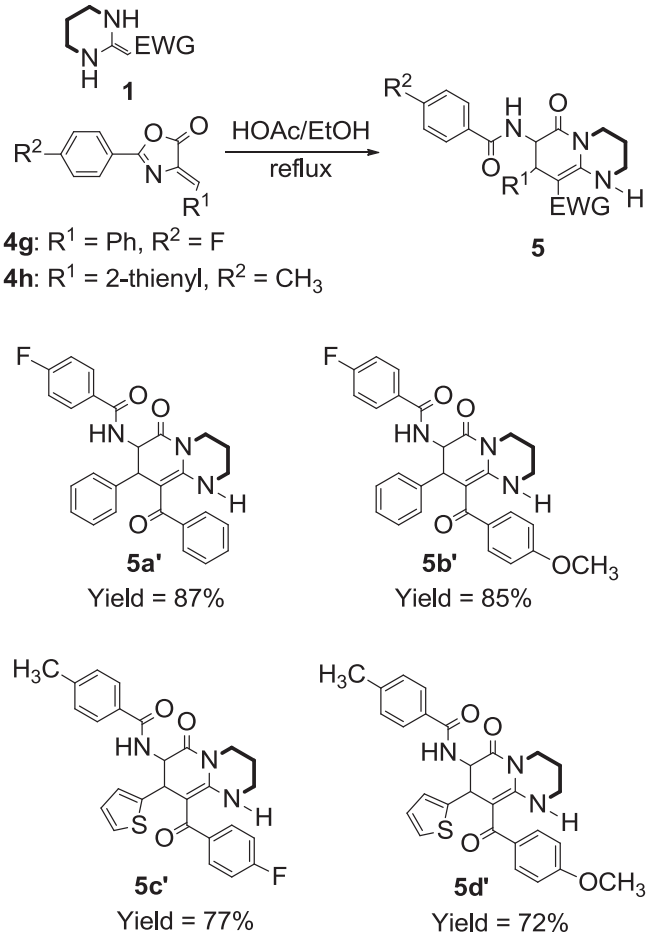
21	 **1e**	 **4e**	 **5u**	76
22	 **1a**	 **4f**	 **5v**	75
23	 **1b**	 **4f**	 **5w**	74
24	 **1c**	 **4f**	 **5x**	75
25	 **1d**	 **4f**	 **5y**	73
26	 **1e**	 **4f**	 **5z**	73

[a] Isolated yield based on HKA**1**.



Scheme 1. Synthesis of bicyclic pyridones.

3. Conclusion

In conclusion, we have successfully demonstrated a novel, efficient, economical, and environmentally friendly method for the synthesis of a series of highly functional bicyclic pyridones via a cascade reaction. The reaction showed that the synthetic route allowed the construction of bicyclic pyridone derivatives with a wide diversity of substituents as important building blocks. Features of this strategy include the mild condition, simple starting material, and excellent yield. Most importantly, this series of pyrido[1,2-*a*]pyrimidin and imidazo[1,2-*a*]pyridine derivatives may provide new classes of biologically active compounds for biomedical screening. Further investigations into the in vitro biological activities of compound **5**–**7** are in progress.

4. Experimental

4.1. General information

All compounds were fully characterised by spectroscopic data. The NMR spectra were recorded on a Bruker DRX500 or DRX400, chemical shifts (δ) are expressed in parts per million, and J values are given in Hertz, and deuterated $CDCl_3$ and DMSO-d_6 were used as solvent. IR spectra were recorded on an FT-IR Thermo Nicolet Avatar 360 using KBr pellet. The reactions were monitored by thin layer chromatography (TLC) using silica gel GF_{254}. The melting points were determined on XT-4A melting point apparatus and are uncorrected. HRMS were performed on an Agilent LC/Msd TOF instrument. All chemicals and solvents were used as received without further purification unless otherwise stated. Column chromatography was performed on silica gel (200–300 mesh).

4.2. Typical procedure for the preparation of bicyclic pyridone 5–7

A mixture of HKAs **1**–**3** (0.22 g, 1 mmol) andarylmethylene-2-phenyloxazol-5(4*H*)-ones **4** (0.25 g, 1 mmol), acetic acid (0.3 mmol) and ethanol (15 mL) was stirred at reflux. Upon completion, monitored by TLC, the reaction mixture was cooled to room temperature and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/ethyl acetate=3:2), which was further purified by recrystallization from mixed EtOAc/$CHCl_3$ to give pure bicyclic pyridones **5**–**7**.

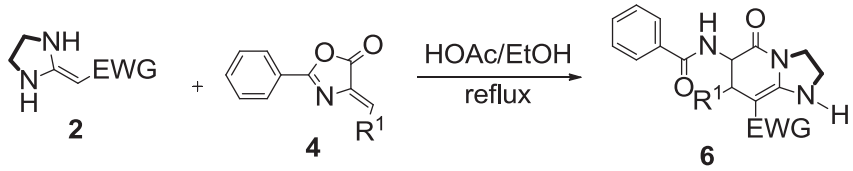
4.2.1. N-(9-(4-Fluorobenzoyl)-6-oxo-8-phenyl2,3,4,6,7,8-hexahydro-1H-pyrido[1,2-a]pyrimidin-7-yl)benzamide ***5a***. White solid; mp 122–124 °C; IR (KBr): 3422, 3060, 1704, 1610, 1238, 1156, 715, 567 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=12.81 (br, 1H, NH), 7.62–7.66 (m, 2H, ArH), 7.45–7.48 (m, 1H, ArH), 7.33–7.42 (m, 2H, ArH), 7.22–7.25 (m, 2H, ArH), 7.02–7.06 (m, 2H, ArH), 6.85–6.89 (m, 4H, ArH), 6.51 (br, 1H, NH), 5.20–5.24 (m, 1H, CH), 4.32 (d, J=6.4 Hz, 1H, CH), 4.11–4.15 (m, 1H, NCH_2), 3.55–3.70 (m, 3H, NCH_2), 2.13–2.17 (m, 2H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ=190.7, 168.1, 167.1, 162.8 (d, J=246.0 Hz), 155.6, 139.0, 137.7, 133.8, 131.9, 128.7, 128.6, 128.4, 128.3, 127.6, 127.0, 114.9 (d, J=21.0 Hz), 114.7 (d, J=21.0 Hz), 90.4, 54.9, 41.7, 39.7, 38.7, 21.0; HRMS (TOF ES^+): m/z calcd for $C_{28}H_{24}FN_3NaO_3$ [$(M+Na)^+$], 492.1694; found, 492.1696.

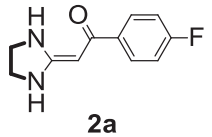
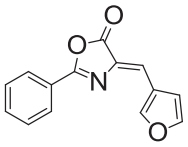
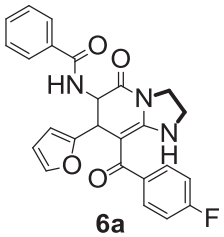
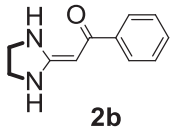
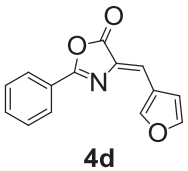
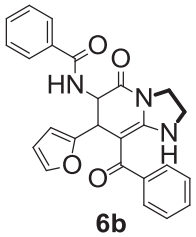
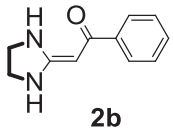
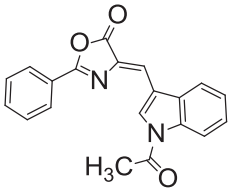
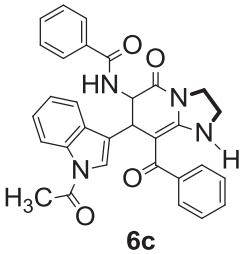
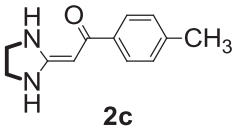
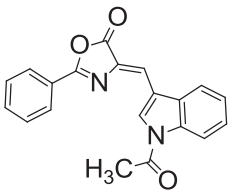
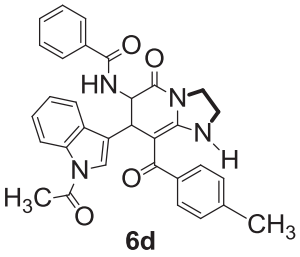
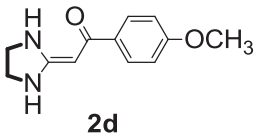
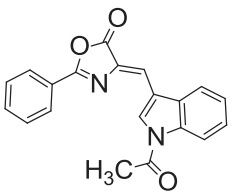
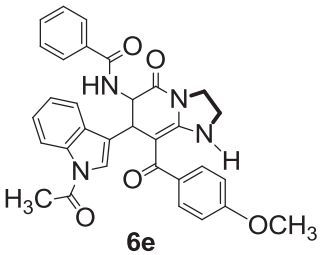
4.2.2. N-(9-(4-Chlorobenzoyl)-6-oxo-8-phenyl-2,3,4,6,7,8-hexahydro-1H-pyrido[1,2-a]pyrimidin-7-yl)benzamide ***5b***. White solid; mp 129–131 °C; IR (KBr): 3787, 3420, 1705, 1657, 1611, 1244, 913, 567 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ=12.82 (br, 1H, NH), 7.66 (d, J=6.8 Hz, 2H, ArH), 7.47–7.50 (m, 1H, ArH), 7.40–7.43 (m, 2H, ArH), 7.22–7.30 (m, 3H, ArH), 7.16–7.20 (m, 2H, ArH), 6.99 (d, J=7.3 Hz, 2H, ArH), 6.85–6.93 (m, 2H, ArH), 6.54 (br, 1H, NH), 5.22–5.26 (m, 1H, CH), 4.31 (d, J=5.6 Hz, 1H, CH), 4.13–4.17 (m, 1H, NCH_2), 3.53–3.77 (m, 3H, NCH_2), 2.14–2.22 (m, 2H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ=190.8, 168.4, 167.5, 156.0, 140.3, 139.4, 135.0, 134.2, 132.3, 129.2, 129.0, 128.7, 128.5, 128.2, 128.0, 127.4, 90.8, 55.3, 42.1, 40.1, 39.1, 21.3; HRMS (TOF ES^+): m/z calcd for $C_{28}H_{25}ClN_3O_3$ [$(M+H)^+$], 486.1579; found, 486.1584.

4.2.3. N-(9-Benzoyl-6-oxo-8-phenyl-2,3,4,6,7,8-hexahydro-1H-pyrido[1,2-a]pyrimidin-7-yl)benzamide ***5c***. White solid; mp 119–120 °C; IR (KBr): 3832, 3425, 1701, 1658, 1614, 1244, 1163, 706 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ=12.86 (br, 1H, NH), 7.65 (d, J=7.5 Hz, 2H, ArH), 7.47–7.51 (m, 1H, ArH), 7.37–7.41 (m, 2H, ArH), 7.24–7.30 (m, 4H, ArH), 7.18–7.23 (m, 3H, ArH), 7.04 (d, J=7.4 Hz, 2H, ArH), 6.85–6.88 (m, 2H, ArH), 6.48 (br, 1H, NH), 5.25–5.28 (m, 1H, CH), 4.33 (d, J=6.5 Hz, 1H, CH), 4.13–4.18 (m, 1H, NCH_2), 3.54–3.77 (m, 3H, NCH_2), 2.16–2.20 (m, 2H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ=192.5, 168.6, 167.5, 155.8, 142.0, 139.6, 134.3, 132.2, 129.1, 128.7, 128.7, 128.3, 127.9, 127.4, 126.6, 90.8, 55.2, 42.2, 40.1, 39.1, 21.4; HRMS (TOF ES^+): m/z calcd for $C_{28}H_{26}N_3O_3$ [$(M+H)^+$], 452.1969; found, 452.1969.

4.2.4. N-(9-(4-Methylbenzoyl)-6-oxo-8-phenyl-2,3,4,6,7,8-hex-ahydro-1H-pyrido[1,2-a]pyrimidin-7-yl)benzamide ***5d***. White solid; mp 117–120 °C; IR (KBr): 3722, 3418, 1704, 1611, 1523, 1327, 1161,

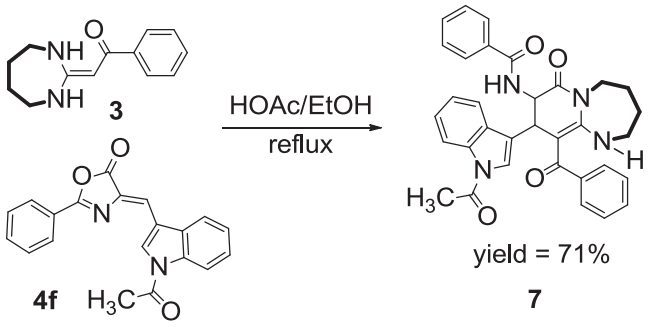
Table 3
Cascade reaction synthesis of products **3** from various of **1** and **2**



Entry	1	2	4	Yield (%)[a]
1				77
2				76
3				73
4				73
5				72

[a] Isolated yield based on HKA**2**.

712 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ=12.89 (br, 1H, NH), 7.66 (d, J=7.5 Hz, 2H, ArH), 7.47–7.51 (m, 1H, ArH), 7.37–7.41 (m, 2H, ArH), 7.25–7.29 (m, 3H, ArH), 6.99–7.03 (m, 2H, ArH), 6.95–6.98 (m, 2H, ArH), 6.89–6.92 (m, 1H, ArH), 6.52 (br, 1H, NH), 5.23–5.27 (m, 1H, CH), 4.38 (d, J=7.4 Hz, 1H, CH), 4.12–4.17 (m, 1H, NCH_2), 3.55–3.72 (m, 3H, NCH_2), 2.30 (s, 3H, CH_3), 2.14–2.17 (m, 2H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ=192.0, 168.1, 167.0, 155.3, 139.2, 138.7, 138.5, 133.9, 131.7, 128.5, 128.4, 127.3, 126.9, 126.2, 124.6, 90.3, 54.7, 43.5,



Scheme 2. Synthesis of bicyclic pyridone **7**.

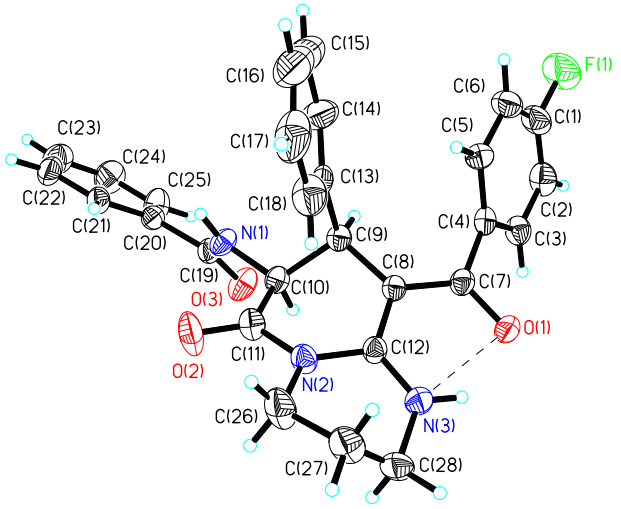
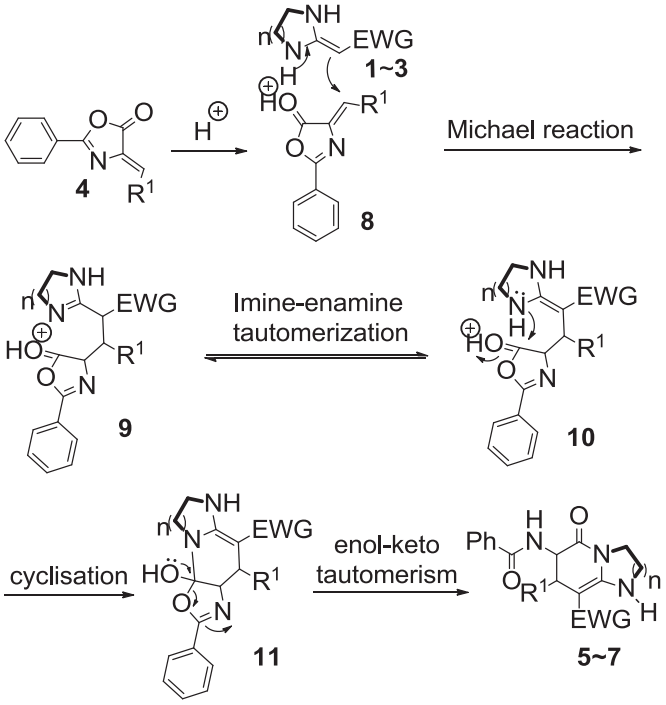


Fig. 2. X-ray crystal structures of **5a**; ellipsoids are drawn at 30% probability level.



Scheme 3. Plausible mechanism for the formation of **5**–**7**.

41.7, 39.6, 38.5, 21.2, 21.0; HRMS (TOF ES$^+$): *m*/*z* calcd for $C_{29}H_{27}N_3NaO_3$ [(M+Na)$^+$], 488.1945; found, 488.1947.

4.2.5. N-(9-(4-Methoxybenzoyl)-6-oxo-8-phenyl-2,3,4,6,7,8-hexahydro-1H-pyrido[1,2-a]pyrimidin-7-yl)benzamide ***5e***. White solid; mp 111–114 °C; IR (KBr): 3792, 3412, 1608, 1525, 1246, 1167, 837, 714 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ=12.90 (br, 1H, NH), 7.68 (d, *J*=7.5 Hz, 2H, ArH), 7.49–7.52 (m, 1H, ArH), 7.39–7.43 (m, 2H, ArH), 7.24–7.30 (m, 3H, ArH), 7.04–7.08 (m, 2H, ArH), 6.90–6.96 (m, 2H, ArH), 6.72 (d, *J*=8.2 Hz, 2H, ArH), 6.54 (br, 1H, NH), 5.23–5.27 (m, 1H, CH), 4.43 (d, *J*=6.1 Hz, 1H, CH), 4.14–4.19 (m, 1H, NCH_2), 3.78 (s, 3H, OCH_3), 3.54–3.75 (m, 3H, NCH_2), 2.16–2.20 (m, 2H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ=192.0, 168.6, 167.5, 160.5, 155.8, 139.7, 134.7, 134.3, 132.2, 129.1, 129.0, 128.8, 128.5, 127.8, 127.4, 113.5, 90.8, 55.6, 55.3, 42.3, 40.1, 39.1, 21.5; HRMS (TOF ES$^+$): *m*/*z* calcd for $C_{29}H_{28}N_3O_4$ [(M+H)$^+$], 482.2074; found, 482.2078.

4.2.6. N-(9-(4-Chlorobenzoyl)-8-(4-methoxyphenyl)-6-oxo-2,3,4,6,7,8-hexahydro-1H-pyrido[1,2-a]pyrimidin-7-yl)benzamide ***5f***. White solid; mp 114–117 °C; IR (KBr): 3775, 3426, 1706, 1655, 1613, 1245, 1171, 802 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ=12.64 (br, 1H, NH), 7.74 (d, *J*=7.6 Hz, 2H, ArH), 7.68 (br, 1H, NH), 7.50–7.54 (m, 1H, ArH), 7.40–7.45 (m, 2H, ArH), 7.29 (d, *J*=8.1 Hz, 1H, ArH), 6.99 (d, *J*=8.1 Hz, 2H, ArH), 6.80–6.84 (m, 2H, ArH), 6.74–6.78 (m, 2H, ArH), 5.17–5.21 (m, 1H, CH), 4.09 (d, *J*=6.2 Hz, 1H, CH), 3.95–4.01 (m, 1H, NCH_2), 3.76 (s, 3H, OCH_3), 3.60–3.70 (m, 3H, NCH_2), 2.06–2.09 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ=187.6, 168.0, 166.7, 158.6, 156.1, 141.2, 134.0, 133.4, 132.0, 131.6, 129.6, 128.8, 128.2, 128.1, 127.7, 114.3, 90.3, 55.4, 55.3, 40.7, 39.8, 38.6, 20.4; HRMS (TOF ES$^+$): *m*/*z* calcd for $C_{29}H_{27}ClN_3O_4$ [(M+H)$^+$], 516.1685; found, 516.1686.

4.2.7. N-(9-Benzoyl-8-(4-methoxyphenyl)-6-oxo-2,3,4,6,7,8-hexahydro-1H-pyrido[1,2-a]pyrimidin-7-yl)benzamide ***5g***. White solid; mp 120–124 °C; IR (KBr): 3730, 3420, 1614, 1512, 1380, 1164, 902, 711 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ=12.70 (br, 1H, NH), 7.73 (d, *J*=7.3 Hz, 1H, ArH), 7.67 (br, 1H, NH), 7.50–7.53 (m, 1H, ArH), 7.40–7.44 (m, 2H, ArH), 7.28–7.30 (m, 1H, ArH), 7.20–7.24 (m, 2H, ArH), 6.96–6.99 (m, 2H, ArH), 6.79–6.81 (m, 2H, ArH), 6.73–6.75 (m, 2H, ArH), 5.16–5.20 (m, 1H, CH), 4.11 (d, *J*=5.8 Hz, 1H, CH), 3.96–4.00 (m, 1H, NCH_2), 3.71 (s, 3H, OCH_3), 3.57–3.65 (m, 3H, NCH_2), 2.05–2.11 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ=189.2, 168.1, 166.7, 158.6, 156.0, 142.4, 134.0, 132.0, 129.6, 128.8, 128.8, 128.0, 127.6, 126.3, 114.2, 90.3, 55.2, 55.2, 40.8, 39.8, 38.6, 21.5; HRMS (TOF ES$^+$): *m*/*z* calcd for $C_{29}H_{28}N_3O_4$ [(M+H)$^+$], 482.2074; found, 482.2079.

4.2.8. N-(9-(4-Methoxybenzoyl)-8-(4-methoxyphenyl)-6-oxo-2,3,4,6,7,8-hexahydro-1H-pyrido[1,2-a]pyrimidin-7-yl)benzam-ide ***5h***. White solid; mp 115–117 °C; IR (KBr): 3788, 3414, 1608, 1512, 1247, 1025, 837, 739 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ=12.79 (br, 1H, NH), 7.75 (d, *J*=7.7 Hz, 2H, ArH), 7.69 (br, 1H, NH), 7.50–7.56 (m, 1H, ArH), 7.40–7.47 (m, 2H, ArH), 6.99–7.03 (m, 2H, ArH), 6.76–6.85 (m, 6H, ArH), 5.16–5.18 (m, 1H, CH), 4.22 (d, *J*=6.1 Hz, 1H, CH), 3.95–4.03 (m, 1H, NCH_2), 3.72 (s, 6H, OCH_3), 3.56–3.72 (m, 3H, NCH_2), 2.04–2.08 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ=189.2, 168.6, 167.2, 160.3, 159.1, 156.4, 135.4, 134.5, 132.5, 132.3, 130.2, 129.3, 128.7, 128.2, 114.8, 113.8, 90.8, 55.9, 55.8, 41.4, 39.8, 39.0, 21.1; HRMS (TOF ES$^+$): *m*/*z* calcd for $C_{30}H_{30}N_3O_5$ [(M+H)$^+$], 512.2180; found, 512.2188.

4.2.9. N-(9-(4-Fluorobenzoyl)-6-oxo-8-(thiophen-2-yl)-2,3,4,6,7,8-hexahydro-1H-pyrido[1,2-a]pyrimidin-7-yl)benzamide ***5i***. White solid; mp 109–110 °C; IR (KBr): 3714, 3425, 1699, 1608, 1489, 1238, 1158, 713 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ=12.73 (br, 1H, NH), 7.78 (d, *J*=7.4 Hz, 2H, ArH), 7.51–7.53 (m, 1H, ArH), 7.42–7.47 (m,

2H, ArH), 7.21–7.27 (m, 2H, ArH), 7.29–7.21 (m, 1H, ArH), 6.95–6.98 (m, 2H, ArH), 6.92–6.94 (m, 1H, ArH), 6.86 (d, *J*=4.9 Hz, 2H, ArH), 6.65 (br, 1H, NH), 5.17–5.20 (m, 1H, CH), 4.67 (d, *J*=5.2 Hz, 1H, CH), 4.08–4.14 (m, 1H, NCH_2), 3.52–3.70 (m, 3H, NCH_2), 2.13–2.19 (m, 2H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ=190.5, 168.3, 167.5, 162.7 (d, *J*=245.0 Hz), 155.6, 143.4, 137.9, 134.1, 132.4, 129.1, 128.9, 127.5, 127.5, 126.2, 125.6, 115.5 (d, *J*=21.3 Hz), 115.4 (d, *J*=21.3 Hz), 92.0, 55.4, 40.2, 39.1, 38.4, 21.3; HRMS (TOF ES^+): *m*/*z* calcd for $C_{26}H_{23}FN_3O_3S$ [$(M+H)^+$], 476.1439; found, 476.1433.

4.2.10. N-(9-(4-Chlorobenzoyl)-6-oxo-8-(thiophen-2-yl)-2,3,4,6,7,8-hexahydro-1H-pyrido[1,2-a]pyrimidin-7-yl)benzamide ***5j***. White solid; mp 207–209 °C; IR (KBr): 3730, 3406, 1704, 1613, 1530, 1242, 903, 724 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ=12.72 (br, 1H, NH), 7.78 (d, *J*=7.1 Hz, 2H, ArH), 7.51–7.55 (m, 1H, Ar–H), 7.43–7.47 (m, 2H, ArH), 7.25–7.29 (m, 3H, ArH), 7.17–7.21 (m, 3H, ArH), 6.92–6.94 (m, 1H, ArH), 6.84–6.86 (m, 1H, ArH), 6.65 (br, 1H, NH), 5.17–5.19 (m, 1H, CH), 4.64 (d, *J*=5.2 Hz, 1H, CH), 4.09–4.13 (m, 1H, NCH_2), 3.52–3.74 (m, 3H, NCH_2), 2.14–2.20 (m, 2H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ=190.3, 168.3, 167.6, 155.7, 143.4, 140.1, 135.4, 134.1, 132.4, 129.1, 128.7, 128.3, 127.5, 127.5, 126.2, 125.6, 92.0, 55.4, 40.2, 39.1, 38.3, 21.3; HRMS (TOF ES^+): *m*/*z* calcd for $C_{26}H_{23}ClN_3O_3S$ [$(M+H)^+$], 492.1143; found, 492.1141.

4.2.11. N-(9-Benzoyl-6-oxo-8-(thiophen-2-yl)-2,3,4,6,7,8-hexa-hydro-1H-pyrido[1,2-a]pyrimidin-7-yl)benzamide ***5k***. White solid; mp 169–171 °C; IR (KBr): 3788, 3435, 1616, 1529, 1240, 1164, 706, 531 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ=12.64 (br, 1H, NH), 7.67 (d, *J*=7.5 Hz, 2H, ArH), 7.41–7.45 (m, 1H, ArH), 7.32–7.36 (m, 2H, ArH), 7.18–7.24 (m, 3H, ArH), 7.14 (d, *J*=6.7 Hz, 2H, ArH), 7.10 (d, *J*=4.7 Hz, 1H, ArH), 6.82–6.84 (m, 1H, ArH), 6.72 (d, *J*=5.9 Hz, 1H, ArH), 6.53 (br, 1H, NH), 5.10–5.14 (m, 1H, CH), 4.56 (d, *J*=5.6 Hz, 1H, CH), 3.99–4.05 (m, 1H, NCH_2), 3.45–3.60 (m, 3H, NCH_2), 2.04–2.10 (m, 2H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ=191.8, 168.4, 167.5, 155.5, 143.6, 141.7, 134.2, 132.3, 129.4, 129.0, 128.4, 127.5, 127.5, 126.7, 126.2, 125.4, 92.0, 55.3, 40.2, 39.1, 38.4, 21.4; HRMS (TOF ES^+): *m*/*z* calcd for $C_{26}H_{24}N_3O_3S$ [$(M+H)^+$], 458.1533; found, 458.1539.

4.2.12. N-(9-(4-Methylbenzoyl)-6-oxo-8-(thiophen-2-yl)-2,3,4,6,7,8-hexahydro-1H-pyrido[1,2-a]pyrimidin-7-yl) benzamide ***5l***. White solid; mp 222–223 °C; IR (KBr): 3832, 3418, 1703, 1659, 1612, 1243, 918, 706 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ=12.77 (br, 1H, NH), 7.78 (d, *J*=7.8 Hz, 2H, ArH), 7.50–7.54 (m, 1H, ArH), 7.42–7.46 (m, 2H, ArH), 7.20 (d, *J*=5.0 Hz, 1H, ArH), 7.15–7.17 (m, 2H, ArH), 7.06–7.10 (m, 2H, ArH), 6.92–6.94 (m, 1H, ArH), 6.84 (d, *J*=5.9 Hz, 1H, ArH), 6.66 (br, 1H, NH), 5.19–5.22 (m, 1H, CH), 4.70 (d, *J*=5.6 Hz, 1H, CH), 4.08–4.14 (m, 1H, NCH_2), 3.50–3.70 (m, 3H, NCH_2), 2.33 (s, 3H, CH_3), 2.13–2.17 (m, 2H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ=192.0, 168.4, 167.5, 155.4, 143.7, 139.3, 138.9, 134.2, 132.3, 129.1, 129.1, 127.5, 127.5, 126.8, 126.1, 125.4, 92.0, 55.4, 40.2, 39.0, 38.5, 21.7, 21.4; HRMS (TOF ES^+): *m*/*z* calcd for $C_{27}H_{26}N_3O_3S$ [$(M+H)^+$], 472.1689; found, 472.1699.

4.2.13. N-(9-(4-Methoxybenzoyl)-6-oxo-8-(thiophen-2-yl)-2,3,4,6,7,8-hexahydro-1H-pyrido[1,2-a]pyrimidin-7-yl) benzamide ***5m***. White solid; mp 116–119 °C; IR (KBr): 3832, 3415, 1674, 1607, 1378, 1243, 1169, 709 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ=12.68 (br, 1H, NH), 7.69 (d, *J*=7.5 Hz, 2H, ArH), 7.41–7.45 (m, 1H, ArH), 7.32–7.36 (m, 2H, ArH), 7.15 (d, *J*=8.4 Hz, 2H, ArH), 7.09 (d, *J*=4.8 Hz, 1H, ArH), 6.82–6.84 (m, 1H, ArH), 6.77–6.79 (m, 1H, ArH), 6.71 (d, *J*=8.4 Hz, 2H, ArH), 6.59 (br, 1H, NH), 5.08–5.11 (m, 1H, CH), 4.67 (d, *J*=5.4 Hz, 1H, CH), 3.97–4.01 (m, 1H, NCH_2), 3.69 (s, 3H, OCH_3), 3.40–3.58 (m, 3H, NCH_2), 2.00–2.06 (m, 2H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ=191.3, 168.4, 167.5, 160.7, 155.4, 143.8, 134.4, 134.3, 132.3, 129.1, 128.7, 127.5, 127.5, 126.2, 125.5, 113.7, 92.0, 55.6, 55.4, 40.2, 39.0, 38.5, 21.4; HRMS (TOF ES^+): *m*/*z* calcd for $C_{27}H_{26}N_3O_4S$ [$(M+H)^+$], 488.1639; found, 488.1645.

4.2.14. N-(9-(4-Fluorobenzoyl)-8-(furan-2-yl)-6-oxo-2,3,4,6,7,8-hexahydro-1H-pyrido[1,2-a]pyrimidin-7-yl)benzamide ***5n***. White solid; mp 212–214 °C; IR (KBr): 3792, 3417, 1706, 1610, 1529, 1235, 1013, 841 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ=12.74 (br, 1H, NH), 7.72 (d, *J*=7.5 Hz, 2H, ArH), 7.49–7.51 (m, 1H, ArH), 7.40–7.44 (m, 2H, ArH), 7.26–7.32 (m, 3H, ArH), 7.01–7.04 (m, 2H, ArH), 6.85 (br, 1H, NH), 6.24–6.28 (m, 1H, ArH), 5.85–5.89 (m, 1H, ArH), 5.16–5.19 (m, 1H, CH), 4.48 (d, *J*=5.6 Hz, 1H, CH), 4.14–4.18 (m, 1H, NCH_2), 3.52–3.68 (m, 3H, NCH_2), 2.11–2.14 (m, 2H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ=190.2, 168.6, 167.7, 163.4 (d, *J*=246.0 Hz), 156.1, 153.9, 142.9, 138.0, 134.3, 132.2, 129.0, 128.9, 127.5, 115.6 (d, *J*=26.6 Hz), 115.4 (d, *J*=26.6 Hz), 107.8, 108.3, 88.9, 54.5, 40.0, 39.1, 37.0, 21.2; HRMS (TOF ES^+): *m*/*z* calcd for $C_{26}H_{23}FN_3O_4$ [$(M+H)^+$], 460.1667; found, 460.1672.

4.2.15. N-(9-(4-Chlorobenzoyl)-8-(furan-2-yl)-6-oxo-2,3,4,6,7,8-hexahydro-1H-pyrido[1,2-a]pyrimidin-7-yl) benzamide ***5o***. White solid; mp 179–180 °C; IR (KBr): 3783, 3223, 1707, 1653, 1610, 1237, 923, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ=12.73 (br, 1H, NH), 7.72 (d, *J*=7.6 Hz, 2H, ArH), 7.49–7.53 (m, 1H, ArH), 7.40–7.44 (m, 2H, ArH), 7.28–7.33 (m, 3H, ArH), 7.31 (t, *J*=9.3 Hz, 2H, ArH), 6.84 (br, 1H, NH), 6.25–6.27 (m, 1H, ArH), 5.87 (d, *J*=2.7 Hz, 1H, ArH), 5.16–5.19 (m, 1H, CH), 4.45 (d, *J*=5.8 Hz, 1H, CH), 4.13–4.19 (m, 1H, NCH_2), 3.53–3.70 (m, 3H, NCH_2), 2.10–2.16 (m, 2H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ=189.9, 168.6, 167.7, 156.1, 153.8, 143.0, 140.2, 135.2, 134.3, 132.3, 129.0, 128.8, 128.3, 127.5, 110.8, 108.4, 88.9, 54.4, 40.0, 39.1, 37.0, 21.2; HRMS (TOF ES^+): *m*/*z* calcd for $C_{26}H_{23}ClN_3O_4$ [$(M+H)^+$], 476.1372; found, 476.1371.

4.2.16. N-(9-Benzoyl-8-(furan-2-yl)-6-oxo-2,3,4,6,7,8-hexahy-dro-1H-pyrido[1,2-a]pyrimidin-7-yl) benzamide ***5p***. White solid; mp 187–189 °C; IR (KBr): 3714, 3426, 1706, 1614, 1524, 1374, 1157, 918 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ=12.76 (br, 1H, NH), 7.98–8.05 (m, 2H, ArH), 7.69–7.73 (m, 1H, ArH), 7.43–7.53 (m, 2H, ArH), 7.30–7.36 (m, 3H, ArH), 7.27–7.31 (m, 3H, ArH), 6.83 (br, 1H, NH), 6.23–6.27 (m, 1H, ArH), 5.83–5.87 (m, 1H, ArH), 5.18–5.22 (m, 1H, CH), 4.44–4.48 (m, 1H, CH), 4.11–4.17 (m, 1H, NCH_2), 3.50–3.67 (m, 3H, NCH_2), 2.06–2.14 (m, 2H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ=191.4, 168.6, 167.7, 156.0, 154.1, 142.9, 141.9, 134.4, 132.2, 129.3, 129.0, 128.6, 127.5, 126.7, 110.8, 108.3, 88.9, 54.4, 40.0, 39.0, 37.0, 21.2; HRMS (TOF ES^+): *m*/*z* calcd for $C_{26}H_{24}N_3O_4$ [$(M+H)^+$], 442.1761; found, 442.1763.

4.2.17. N-(8-(Furan-2-yl)-9-(4-methylbenzoyl)-6-oxo-2,3,4,6,7,8-hexahydro-1H-pyrido[1,2-a]pyrimidin-7-yl) benzamide ***5q***. White solid; mp 237–239 °C; IR (KBr): 3783, 3425, 1705, 1611, 1523, 1238, 821, 702 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ=12.57 (br, 1H, NH), 7.99 (br, 1H, NH), 7.78 (d, *J*=6.9 Hz, 2H, ArH), 7.53–7.55 (m, 1H, ArH), 7.46–7.50 (m, 1H, ArH), 7.44–7.47 (m, 2H, ArH), 7.12–7.15 (m, 2H, ArH), 7.05–7.08 (m, 2H, ArH), 6.31–6.35 (m, 1H, ArH), 5.95–5.99 (m, 1H, ArH), 5.17–5.21 (m, 1H, CH), 4.30–4.37 (m, 1H, CH), 3.95–4.05 (m, 1H, NCH_2), 3.52–3.62 (m, 3H, NCH_2), 2.29 (s, 3H, CH_3), 1.99–2.05 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ=188.8, 168.1, 166.8, 155.8, 154.4, 143.0, 139.6, 138.4, 134.1, 131.9, 128.8, 128.7, 128.7, 127.8, 126.5, 110.7, 107.4, 88.4, 54.5, 39.7, 38.5, 36.7, 21.2, 20.5; HRMS (TOF ES^+): *m*/*z* calcd for $C_{27}H_{26}N_3O_4$ [$(M+H)^+$], 456.1918; found, 456.1915.

4.2.18. N-(8-(Furan-2-yl)-9-(4-methoxybenzoyl)-6-oxo-2,3,4,6,7,8-hexahydro-1H-pyrido[1,2-a]pyrimidin-7-yl)benzamide ***5r***. White solid; mp 231–232 °C; IR (KBr): 3788, 3217, 1705, 1649, 1607, 1164, 927, 768 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ=12.77 (br, 1H, NH), 7.72 (d, *J*=7.3 Hz, 2H, ArH), 7.47–7.51 (m, 1H, ArH), 7.38–7.42 (m,

2H, ArH), 7.24–7.27 (m, 2H, ArH), 6.82–6.85 (m, 2H, ArH), 6.25 (t, J=2.4 Hz, 1H, ArH), 5.89 (d, J=3.0 Hz, 1H, ArH), 5.16–5.20 (m, 1H, CH), 4.56 (d, J=5.8 Hz, 1H, CH), 4.11–4.18 (m, 1H, NCH_2), 3.79 (s, 3H, OCH_3), 3.48–3.65 (m, 3H, NCH_2), 2.04–2.10 (m, 2H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ=191.2, 168.2, 167.3, 155.4, 153.8, 142.4, 134.0, 131.7, 128.5, 128.5, 128.1, 127.0, 113.3, 110.3, 107.8, 88.5, 55.1, 54.0, 39.5, 38.5, 36.7, 20.8; HRMS (TOF ES$^+$): m/z calcd for $C_{27}H_{26}N_3O_5$ [(M+H)$^+$], 472.1867; found, 472.1877.

4.2.19. N-(9-(4-Chlorobenzoyl)-8-(5-methylfuran-2-yl)-6-oxo-2,3,4,6,7,8-hexahydro-1H-pyrido[1,2-a]pyrimidin-7-yl) benz-amide ***5s***. White solid; mp 203–204 °C; IR (KBr): 3729, 3337, 1712, 1622, 1245, 1164, 788, 706 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ=12.48 (br, 1H, NH), 8.07 (br, 1H, NH), 7.77–7.85 (m, 2H, ArH), 7.51–7.55 (m, 1H, ArH), 7.40–7.48 (m, 2H, ArH), 7.37–7.45 (m, 2H, ArH), 5.91–5.95 (m, 1H, ArH), 5.85–5.91 (m, 1H, ArH), 5.15–5.21 (m, 1H, CH), 4.12–4.15 (m, 1H, CH), 3.93–4.01 (m, 1H, NCH_2), 3.50–3.61 (m, 3H, NCH_2), 2.13 (s, 3H, CH_3), 1.99–2.05 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ=187.1, 168.0, 166.8, 156.0, 152.3, 151.6, 141.0, 134.1, 133.5, 131.9, 128.7, 128.7, 128.4, 128.4, 127.8, 108.2, 106.7, 88.4, 54.5, 39.4, 38.6, 36.6, 20.4, 13.6; HRMS (TOF ES$^+$): m/z calcd for $C_{27}H_{25}ClN_3O_4$ [(M+H)$^+$], 490.1528; found, 490.1538.

4.2.20. N-(9-Benzoyl-8-(5-methylfuran-2-yl)-6-oxo-2,3,4,6,7,8-hexahydro-1H-pyrido[1,2-a]pyrimidin-7-yl) benzamide ***5t***. White solid; mp 205–207 °C; IR (KBr): 3787, 3402, 1702, 1653, 1613, 1245, 1171, 802 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ=12.77 (br, 1H, NH), 7.74 (d, J=7.5 Hz, 2H, ArH), 7.47–7.52 (m, 1H, ArH), 7.39–7.44 (m, 2H, ArH), 7.31–7.35 (m, 3H, ArH), 7.27–7.31 (m, 2H, ArH), 6.86 (br, 1H, NH), 5.82–5.86 (m, 1H, ArH), 5.80 (d, J=6.9 Hz, 1H, ArH), 5.18–5.22 (m, 1H, CH), 4.34 (d, J=5.6 Hz, 1H, CH), 4.12–4.19 (m, 1H, NCH_2), 3.53–3.65 (m, 3H, NCH_2), 2.56 (s, 3H, CH_3), 2.11–2.14 (m, 2H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ=191.3, 168.7, 167.6, 156.1, 152.4, 152.2, 141.9, 134.5, 132.1, 129.3, 129.0, 128.5, 127.5, 126.7, 109.2, 106.7, 89.1, 54.4, 40.0, 39.0, 37.1, 21.3, 14.0; HRMS (TOF ES$^+$): m/z calcd for $C_{27}H_{26}N_3O_4$ [(M+H)$^+$], 456.1918; found, 456.1923.

4.2.21. N-(9-(4-Methoxybenzoyl)-8-(5-methylfuran-2-yl)-6-oxo-2,3,4,6,7,8-hexahydro-1H-pyrido[1,2-a]pyrimidin-7-yl)benz-amide ***5u***. White solid; mp 189–192 °C; IR (KBr): 3440, 3363, 1691, 1644, 1524, 1245, 787, 608 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=12.70 (br, 1H, NH), 7.67 (d, J=7.3 Hz, 2H, ArH), 7.39–7.44 (m, 1H, ArH), 7.31–7.36 (m, 2H, ArH), 7.19–7.24 (m, 3H, ArH), 6.80 (br, 1H, NH), 5.75 (d, J=1.8 Hz, 2H, ArH), 5.10 (t, J=6.4 Hz, 1H, CH), 4.35 (d, J=5.6 Hz, 1H, CH), 4.03–4.09 (m, 1H, NCH_2), 3.72 (s, 3H, OCH_3), 3.40–3.55 (m, 3H, NCH_2), 2.12 (s, 3H, CH_3), 1.98–2.06 (m, 2H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ=189.5, 167.3, 166.2, 159.1, 154.5, 151.0, 150.9, 133.1, 130.7, 127.5, 127.5, 127.2, 126.1, 112.4, 107.8, 105.3, 87.7, 54.2, 53.1, 38.5, 37.6, 35.8, 19.9, 12.6; HRMS (TOF ES$^+$): m/z calcd for $C_{28}H_{28}N_3O_5$[(M+H)$^+$], 486.2023; found, 486.2033.

4.2.22. N-(8-(1-Acetyl-1H-indol-3-yl)-9-(4-fluorobenzoyl)-6-oxo-2,3,4,6,7,8-hexahydro-1H-pyrido[1,2-a]pyrimidin-7-yl)-benzamide ***5v***. White solid; mp 265–268 °C; IR (KBr): 3796, 3400, 1703, 1612, 1378, 1273, 845, 749 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ=12.63 (br, 1H, NH), 8.27 (br, 1H, NH), 7.92–8.00 (m, 1H, ArH), 7.52–7.60 (m, 2H, ArCH), 7.40–7.46 (m, 1H, ArCH), 7.29–7.38 (m, 3H, ArCH), 7.13–7.23 (m, 3H, ArCH), 6.92–7.02 (m, 3H, ArCH), 6.80–6.86 (m, 1H, ArCH), 5.29–5.33 (m, 1H, CH), 4.49–4.52 (m, 1H, CH), 4.02–4.08 (m, 1H, NCH), 3.59–3.76 (m, 2H, NCH_2), 2.60 (s, 3H, CH_3), 2.08–2.16 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ=187.2, 169.7, 168.2, 167.3, 162.3 (d, J=243.7 Hz), 155.9, 138.7, 135.3, 134.1, 131.7, 130.6, 128.8, 128.4, 128.4, 127.8, 125.0, 124.4, 123.2, 121.6, 118.8, 116.2, 115.1 (d, J=21.3 Hz), 114.9 (d, J=21.3 Hz), 90.5, 55.7, 39.7, 38.7, 33.6, 24.2, 20.5; HRMS (TOF ES$^+$): m/z calcd for $C_{32}H_{28}FN_4O_4$ [(M+H)$^+$], 551.2089; found, 551.2091.

4.2.23. N-(8-(1-Acetyl-1H-indol-3-yl)-9-(4-chlorobenzoyl)-6-oxo-2,3,4,6,7,8-hexahydro-1H-pyrido[1,2-a]pyrimidin-7-yl)-benzamide ***5w***. White solid; mp 269–271 °C; IR (KBr): 3824, 3426, 1670, 1615, 1531, 1379, 1005, 752 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ=12.81 (br, 1H, NH), 8.33 (br, 1H, NH), 7.40–7.49 (m, 3H, ArH), 7.27–7.34 (m, 3H, ArH), 7.07–7.16 (m, 6H, ArH), 6.98–7.03 (m, 1H, ArH), 6.62 (d, J=6.1 Hz, 1H, ArH), 5.29–5.32 (m, 1H, CH), 4.73 (d, J=5.8 Hz, 1H, CH), 4.20–4.28 (m, 1H, NCH_2), 3.59–3.72 (m, 3H, NCH_2), 2.56 (s, 3H, CH_3), 1.95–2.22 (m, 2H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ=189.9, 168.6, 168.4, 168.0, 155.6, 139.9, 135.5, 133.9, 132.2, 130.3, 128.8, 128.7, 128.3, 127.5, 126.1, 124.2, 123.2, 122.4, 119.8, 116.6, 91.2, 56.0, 40.1, 39.1, 34.1, 24.5, 21.5; HRMS (TOF ES$^+$): m/z calcd for $C_{32}H_{28}ClN_4O_4$ [(M+H)$^+$], 567.1794; found, 567.1791.

4.2.24. N-(8-(1-Acetyl-1H-indol-3-yl)-9-benzoyl-6-oxo-2,3,4,6,7,8-hexahydro-1H-pyrido[1,2-a]pyrimidin-7-yl)benzamide ***5x***. White solid; mp 277–279 °C; IR (KBr): 3828, 3416, 1702, 1619, 1380, 1244, 702, 539 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ=12.67 (br, 1H, NH), 8.26 (br, 1H, NH), 7.92 (d, J=6.9 Hz, 1H, ArH), 7.51–7.54 (m, 2H, ArH), 7.41–7.47 (m, 1H, ArH), 7.24–7.39 (m, 5H, ArH), 7.10–7.23 (m, 4H, ArH), 6.85–6.91 (m, 1H, ArH), 6.74–6.81 (m, 1H, ArH), 5.28–5.32 (m, 1H, CH), 4.53 (d, J=6.0 Hz, 1H, CH), 4.18–4.22 (m, 1H, NCH_2), 3.43–3.54 (m, 3H, NCH_2), 2.61 (s, 3H, CH_3), 2.08–2.16 (m, 2H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6): δ=188.5, 169.8, 168.3, 167.3, 156.0, 142.3, 135.4, 134.2, 131.8, 130.8, 128.9, 128.5, 128.2, 127.9, 126.5, 125.3, 124.3, 123.3, 121.9, 119.0, 116.2, 90.6, 55.8, 39.4, 38.7, 33.6, 22.4, 20.6; HRMS (TOF ES$^+$): m/z calcd for $C_{32}H_{29}N_4O_4$ [(M+H)$^+$], 533.2183; found, 533.2184.

4.2.25. N-(8-(1-Acetyl-1H-indol-3-yl)-9-(4-methylbenzoyl)-6-oxo-2,3,4,6,7,8-hexahydro-1H-pyrido[1,2-a]pyrimidin-7-yl)-benzamide ***5y***. White solid; mp 263–266 °C; IR (KBr): 3726, 3418, 1703, 1614, 1378, 1169, 927, 747 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ=12.85 (br, 1H, NH), 8.33 (br, 1H, NH), 7.42–7.45 (m, 3H, ArH), 7.26–7.31 (m, 3H, ArH), 7.08–7.12 (m, 4H, ArH), 6.97–7.00 (m, 1H, ArH), 6.93 (d, J=7.0 Hz, 2H, ArH), 6.56–6.59 (m, 1H, ArH), 5.31–5.34 (m, 1H, CH), 4.78 (d, J=5.0 Hz, 1H, CH), 4.20–4.24 (m, 1H, NCH_2), 3.54–3.62 (m, 3H, NCH_2), 2.25 (s, 3H, CH_3), 2.13–2.21 (m, 2H, CH_2), 1.77 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ=191.7, 168.8, 168.5, 168.0, 155.3, 139.5, 138.7, 136.1, 134.0, 132.1, 130.5, 129.1, 128.8, 127.5, 126.8, 125.9, 124.0, 123.2, 122.7, 120.0, 116.6, 91.3, 56.0, 40.1, 39.1, 34.2, 24.4, 21.6; HRMS (TOF ES$^+$): m/z calcd for $C_{33}H_{31}N_4O_4$ [(M+H)$^+$], 547.2340; found, 547.2340.

4.2.26. N-(8-(1-Acetyl-1H-indol-3-yl)-9-(4-methoxybenzoyl)-6-oxo-2,3,4,6,7,8-hexahydro-1H-pyrido[1,2-a]pyrimidin-7-yl) benzamide ***5z***. White solid; mp 256–258 °C; IR (KBr): 3714, 3305, 1712, 1696, 1602, 1250, 924, 751 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ=12.78 (br, 1H, NH), 8.29 (br, 1H, NH), 7.37–7.42 (m, 3H, ArH), 7.21–7.27 (m, 3H, ArH), 7.14 (d, J=6.1 Hz, 2H, ArH), 7.07–7.10 (m, 2H, ArH), 6.93–6.96 (m, 1H, ArH), 6.58–6.63 (m, 3H, ArH), 5.24–5.28 (m, 1H, CH), 4.77 (d, J=5.0 Hz, 1H, CH), 4.16–4.22 (m, 1H, NCH_2), 3.68 (s, 3H, OCH_3), 3.53–3.61 (m, 3H, NCH_2), 2.38 (s, 3H, CH_3), 2.07–2.17 (m, 2H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ=190.8, 168.7, 168.0, 160.7, 155.3, 136.0, 134.1, 134.0, 132.1, 130.4, 128.8, 128.6, 127.5, 125.9, 124.0, 123.3, 122.6, 119.9, 116.6, 113.7, 91.2, 56.0, 55.6, 40.3, 34.3, 24.4, 21.5; HRMS (TOF ES$^+$): m/z calcd for $C_{33}H_{31}N_4O_5$ [(M+H)$^+$], 563.2289; found, 563.2284.

4.2.27. N-(9-Benzoyl-6-oxo-8-phenyl-2,3,4,6,7,8-hexahydro-1H-pyrido[1,2-a]pyrimidin-7-yl)-4-fluorobenzamide ***5a′***. White solid; mp 220–221 °C; IR (KBr): 3411, 3064, 1613, 1381, 1241, 1163, 703, 505 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=12.81 (br, 1H, NH),

7.61–7.65 (m, 2H, ArH), 7.15–7.26 (m, 6H, ArH), 7.00–7.06 (m, 4H, ArH), 6.81–6.83 (m, 2H, ArH), 6.41 (br, 1H, NH), 5.21 (t, *J*=6.6 Hz, 1H, CH), 4.29 (d, *J*=6.6 Hz, 1H, CH), 4.09–4.15 (m, 1H, NCH_2), 3.74 (s, 3H, OCH_3), 3.51–3.71 (m, 3H, NCH_2), 2.12–2.17 (m, 2H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): *δ*=192.0, 168.1, 164.9 (d, *J*=251.0 Hz), 166.0, 155.4, 141.5, 139.2, 130.0, 129.4, 129.3, 128.7, 128.7, 128.3, 127.9, 127.5, 126.1, 115.8 (d, *J*=22.0 Hz), 115.5 (d, *J*=22.0 Hz), 90.3, 54.8, 41.8, 39.7, 38.7, 20.9; HRMS (TOF ES^+): *m*/*z* calcd for $C_{28}H_{25}FN_3O_3$ $[(M+H)^+]$, 470.1847; found, 470.1850.

4.2.28. 4-Fluoro-N-(9-(4-methoxybenzoyl)-6-oxo-8-phenyl-2,3,4,6,7,8-hexahydro-1H-pyrido[1,2-a]pyrimidin-7-yl)benzamide ***5b′***. White solid; mp>300 °C; IR (KBr): 3415, 3232, 1704, 1528, 1238, 1029, 844, 567 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ*=12.86 (br, 1H, NH), 7.63–7.67 (m, 2H, ArH), 7.23–7.26 (m, 3H, ArH), 7.02–7.08 (m, 4H, ArH), 6.88–6.91 (m, 2H, ArH), 6.70 (d, *J*=8.6 Hz, 2H, ArH), 6.47 (br, 1H, NH), 5.20 (t, *J*=6.5 Hz, 1H, CH), 4.39 (d, *J*=6.5 Hz, 1H, CH), 4.09–4.16 (m, 1H, NCH_2), 3.74 (s, 3H, OCH_3), 3.51–3.69 (m, 3H, NCH_2), 2.14–2.18 (m, 2H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): *δ*=191.5, 168.1, 164.9 (d, *J*=251.0 Hz), 166.0, 160.1, 155.3, 139.2, 134.2, 130.1, 129.4, 129.3, 128.7, 128.4, 128.1, 127.5, 115.8 (d, *J*=22.0 Hz), 115.6 (d, *J*=22.0 Hz), 90.4, 55.2, 55.0, 41.8, 39.7, 38.6, 21.0; HRMS (TOF ES^+): *m*/*z* calcd for $C_{29}H_{27}FN_3O_4$ $[(M+H)^+]$, 500.1980; found, 500.1985.

4.2.29. N-(9-(4-Fluorobenzoyl)-6-oxo-8-(thiophen-2-yl)-2,3,4,6,7,8-hexahydro-1H-pyrido[1,2-a]pyrimidin-7-yl)-4-methylbenz-amide ***5c′***. White solid; mp 267–269 °C; IR (KBr): 3420, 3252, 1704, 1605, 1493, 1235, 1142, 842 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ*=7.66 (d, *J*=7.7 Hz, 2H, ArH), 7.16–7.26 (m, 5H, ArH), 6.89–6.97 (m, 3H, ArH), 6.77–6.81 (m, 1H, ArH), 6.62 (br, 1H, NH), 5.16 (t, *J*=5.6 Hz, 1H, CH), 4.64 (d, *J*=5.4 Hz, 1H, CH), 4.06–4.12 (m, 1H, NCH_2), 3.50–3.67 (m, 3H, NCH_2), 2.38 (s, 3H, CH_3), 2.00–2.08 (m, 2H, CH_2), 1.67 (br, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): *δ*=190.1, 168.0, 167.1, 163.0 (d, *J*=247.0 Hz), 155.2, 143.1, 142.5, 137.5, 130.9, 129.3, 128.5, 128.4, 127.1, 127.1, 125.8, 125.1, 115.1 (d, *J*=21.0 Hz), 114.9 (d, *J*=21.0 Hz), 91.6, 55.0, 39.8, 38.7, 38.0, 21.5, 21.3; HRMS (TOF ES^+): *m*/*z* calcd for $C_{27}H_{25}FN_3O_3S$ $[(M+H)^+]$, 490.1595; found, 490.1592.

4.2.30. N-(9-(4-Methoxybenzoyl)-6-oxo-8-(thiophen-2-yl)-2,3,4,6,7,8-hexahydro-1H-pyrido[1,2-a]pyrimidin-7-yl)-4-methylbenz-amide ***5d′***. White solid; mp>300 °C; IR (KBr): 3418, 2933, 1610, 1374, 1243, 1167, 903, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ*=7.67 (d, *J*=8.0 Hz, 2H, ArH), 7.23 (d, *J*=8.4 Hz, 4H, ArH), 7.16 (d, *J*=5.0 Hz, 1H, ArH), 6.88–6.92 (m, 1H, ArH), 6.76–6.83 (m, 3H, ArH), 6.65 (br, 1H, NH), 5.16 (t, *J*=5.9 Hz, 1H, CH), 4.73 (d, *J*=5.6 Hz, 1H, CH), 4.06–4.12 (m, 1H, NCH_2), 3.77 (s, 3H, OCH_3), 3.49–3.66 (m, 3H, NCH_2), 2.39 (s, 3H, CH_3), 2.10–2.15 (m, 2H, CH_2), 1.67 (br, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): *δ*=191.0, 168.1, 167.0, 160.2, 155.0, 143.4, 142.4, 134.0, 131.0, 129.3, 128.2, 127.1, 125.7, 125.0, 113.3, 91.7, 55.2, 55.0, 39.8, 38.6, 38.1, 21.5, 21.0; HRMS (TOF ES^+): *m*/*z* calcd for $C_{28}H_{28}N_3O_4S$ $[(M+H)^+]$, 502.1795; found, 502.1795.

4.2.31. N-(8-(4-Fluorobenzoyl)-7-(furan-2-yl)-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)benzamide ***6a***. White solid; mp 226–229 °C; IR (KBr): 3869, 3332, 1699, 1641, 1266, 1154, 1107, 847 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): *δ*=9.66 (br, 1H, NH), 7.68 (d, *J*=7.6 Hz, 2H, ArH), 7.48–7.52 (m, 1H, ArH), 7.38–7.42 (m, 2H, ArH), 7.26–7.35 (m, 3H, ArH), 7.01–7.05 (m, 2H, ArH), 6.73 (br, 1H, ArH), 6.20–6.26 (m, 1H, ArH), 5.81 (d, *J*=2.8 Hz, 1H, ArH), 5.17–5.21 (m, 1H, CH), 4.66 (d, *J*=6.2 Hz, 1H, CH), 4.14–4.19 (m, 1H, NCH_2), 3.90–4.01 (m, 3H, NCH_2); ^{13}C NMR (125 MHz, $CDCl_3$): *δ*=191.4, 167.9, 167.1, 163.8 (d, *J*=249.0 Hz), 156.8, 153.8, 142.9, 137.2, 134.3, 132.3, 129.2 (d, *J*=7.5 Hz), 129.2 (d, *J*=7.5 Hz), 129.0, 127.5, 115.7 (d, *J*=21.3 Hz), 115.5 (d, *J*=21.3 Hz), 110.8, 108.3, 87.3, 54.9, 43.6, 42.8, 37.7; HRMS (TOF ES^+): *m*/*z* calcd for $C_{25}H_{21}FN_3O_4$ $[(M+H)^+]$, 446.1511; found, 446.1504.

4.2.32. N-(8-Benzoyl-7-(furan-2-yl)-5-oxo-1,2,3,5,6,7-hexahy-droimidazo[1,2-a]pyridin-6-yl) benzamide ***6b′***. White solid; mp 105–108 °C; IR (KBr): 3788, 3423, 1699, 1636, 1522, 1273, 1017, 708 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): *δ*=9.66 (br, 1H, NH), 7.69 (d, *J*=7.7 Hz, 2H, ArH), 7.49–7.53 (m, 1H, ArH), 7.39–7.43 (m, 2H, ArH), 7.28–7.39 (m, 6H, ArH), 6.73 (br, 1H, NH), 6.23–6.25 (m, 1H, ArH), 5.79–5.81 (m, 1H, ArH), 5.22–5.26 (m, 1H, CH), 4.66 (d, *J*=6.0 Hz, 1H, CH), 4.15–4.19 (m, 1H, NCH_2), 3.92–4.05 (m, 3H, NCH_2); ^{13}C NMR (125 MHz, $CDCl_3$): *δ*=192.3, 167.4, 166.7, 156.1, 153.5, 142.3, 140.6, 133.8, 131.7, 129.4, 128.5, 128.1, 127.0, 126.4, 110.3, 107.8, 86.9, 54.3, 43.0, 42.3, 37.2; HRMS (TOF ES^+): *m*/*z* calcd for $C_{25}H_{22}N_3O_4$ $[(M+H)^+]$, 428.1605; found, 428.1601.

4.2.33. N-(7(-Acetyl-1H-indole-3-yl)-8-benzoyl-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridine-6-yl) benzamide ***6c′***. White solid; mp 213–214 °C; IR (KBr): 3726, 3425, 1699, 1638, 1524, 1258, 1012, 747 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): *δ*=9.68 (br, 1H, NH), 8.24–8.27 (m, 1H, ArH), 8.10 (d, *J*=7.3 Hz, 1H, ArH), 7.49 (d, *J*=7.6 Hz, 2H, ArH), 7.40–7.44 (m, 1H, ArH), 7.26–7.32 (m, 3H, ArH), 7.16–7.22 (m, 5H, ArH), 6.86–6.89 (m, 1H, ArH), 6.79–6.83 (m, 1H, ArH), 5.30–5.33 (m, 1H, CH), 4.61 (d, *J*=6.8 Hz, 1H, CH), 4.03–4.09 (m, 1H, NCH_2), 3.79–3.99 (m, 3H, NCH_2), 2.59 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): *δ*=189.7, 170.0, 167.6, 167.1, 156.1, 141.7, 135.3; 134.1, 131.7, 130.7, 129.4, 128.3, 128.2, 127.8, 126.6, 124.9, 124.1, 123.2, 122.2, 118.9, 116.1, 88.4, 55.9, 43.7, 42.4, 34.3, 24.3; HRMS (TOF ES^+): *m*/*z* calcd for $C_{31}H_{27}N_4O_4$ $[(M+H)^+]$, 519.2027; found, 519.2028.

4.2.34. N-(7(-Acetyl-1H-indole-3-yl)-8-(4-methylbenzoyl)-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridine-6-yl) benz-amide ***6d′***. White solid; mp 270–272 °C; IR (KBr): 3734, 3433, 1702, 1640, 1525, 1264, 927, 750 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): *δ*=9.67 (br, 1H, NH), 8.33 (br, 1H, NH), 7.40–7.43 (m, 3H, ArH), 7.24–7.29 (m, 3H, ArH), 7.12–7.18 (m, 4H, ArH), 6.98–7.01 (m, 1H, ArH), 6.93–6.96 (m, 2H, ArH), 6.56 (d, *J*=6.5 Hz, 1H, ArH), 5.32–5.36 (m, 1H, CH), 4.91 (d, *J*=6.1 Hz, 1H, CH), 4.19–4.22 (m, 1H, NCH_2), 3.90–3.97 (m, 3H, NCH_2CH_2N), 2.56 (s, 3H, CH_3), 2.26 (s, 3H, CH_3) ^{13}C NMR (125 MHz, $CDCl_3$): *δ*=192.5, 168.7, 168.2, 167.4, 156.0, 140.3, 138.0; 136.1, 133.9, 132.2, 130.4, 129.1, 128.8, 127.5, 127.1, 125.9, 124.1, 123.2, 122.6, 119.9, 116.7, 89.6, 56.5, 43.7, 42.9, 35.0, 24.4, 21.7; HRMS (TOF ES^+): *m*/*z* calcd for $C_{32}H_{29}N_4O_4$ $[(M+H)^+]$, 533.2183; found, 533.2188.

4.2.35. N-(7-(1-Acetyl-1H-indol-3-yl)-8-(4-methoxybenzoyl)-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)benz-amide ***6e***. White solid; mp 234–237 °C; IR (KBr): 3788, 3427, 1699, 1638, 1253, 1168, 735, 657 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$+DMSO-d_6): *δ*=9.21 (br, 1H, NH), 7.86 (br, 1H, NH), 6.99 (d, *J*=7.6 Hz, 2H, ArH), 6.97–6.81 (m, 1H, ArH), 6.77–6.85 (m, 3H, ArH), 6.71–6.81 (m, 4H, ArH), 6.62–6.66 (m, 1H, ArH), 6.48–6.52 (m, 1H, ArH), 6.17 (d, *J*=8.6 Hz, 2H, ArH), 4.82–4.86 (m, 1H, CH), 4.35–4.39 (m, 1H, CH), 3.71–3.75 (m, 1H, NCH_2), 3.42–3.58 (m, 3H, NCH_2), 3.26 (s, 3H, OCH_3), 2.12 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$+DMSO-d_6): *δ*=192.7, 177.6, 169.8, 168.0, 167.0, 161.8, 159.4, 135.1, 133.4, 131.8, 129.9, 128.3, 127.5, 126.0, 125.3, 123.4, 123.3, 120.4, 118.5, 116.2, 114.0, 93.2, 55.5, 55.1, 45.2, 43.1, 34.0, 24.0; HRMS (TOF ES^+): *m*/*z* calcd for $C_{32}H_{29}N_4O_5$ $[(M+H)^+]$, 549.2132; found, 549.2139.

4.2.36. N-(9-(1-Acetyl-1H-indol-3-yl)-10-benzoyl-7-oxo-1,2,3,4,5,7,8,9-octahydropyrido[1,2-a][1,3]diazepin-8-yl) benzam-ide ***7***. White solid; mp 287–289 °C; IR (KBr): 3783, 3417, 1703, 1613, 1381, 1242, 1155, 750 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): *δ*=11.77 (br, 1H, NH), 8.26 (br, 1H, NH), 7.54 (d, *J*=7.5 Hz, 3H, ArH), 7.43–7.47 (m, 1H, ArH), 7.30–7.34 (m, 3H, ArH), 7.20–7.26 (m, 3H, ArH), 7.14–7.20 (m,

3H, ArH), 6.85–6.89 (m, 1H, ArH), 6.79–6.82 (m, 1H, ArH), 5.30–5.34 (m, 1H, CH), 4.61 (d, J=5.1 Hz, 1H, CH), 4.49–4.54 (m, 1H, NCH_2), 3.41–3.71 (m, 3H, NCH_2), 2.60 (s, 3H, CH_3), 1.91–1.98 (m, 2H, CH_2), 1.72–1.80 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ=190.4, 169.7, 169.2, 167.1, 161.4, 141.9, 134.0, 131.8, 130.5, 129.5, 128.5, 128.2, 127.7, 126.5, 125.2, 124.3, 123.2, 120.7, 119.0, 116.2, 95.4, 56.3, 45.6, 34.0, 26.2, 24.3; HRMS (TOF ES^+): m/z calcd for $C_{33}H_{31}N_4O_4$ [$(M+H)^+$], 547.2340; found, 547.2341.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.08.052.

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24. CCDC 953332 (**5a**) contains all crystallographic details of this publication and is available free of charge at www.ccdc.cam.ac.uk/consts/retrieving.html or can be ordered from the following address: Cambridge Crystallographic Data Centre, 12 Union Road, GB-Cambridge CB21EZ; fax: +44 1223 336 033; or deposit@ccdc.cam.ac.uk.